

Network Systems
Science & Advanced
Computing
Biocomplexity Institute
& Initiative
University of Virginia

Foresight and Analysis of Infectious Disease Threats to Virginia's Public Health

June 8th, 2023

(data current to June 1st – June 7th)

Biocomplexity Institute Technical report: TR BI-2023-149



BIOCOMPLEXITY INSTITUTE

biocomplexity.virginia.edu

About Us

- Biocomplexity Institute at the University of Virginia
 - Using big data and simulations to understand massively interactive systems and solve societal problems
- Over 20 years of crafting and analyzing infectious disease models
 - Pandemic response for Influenza, Ebola, Zika, and others



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Overview

- **Goal:** Understand impact of current and emerging Infectious Disease threats to the Commonwealth of Virginia using modeling and analytics
- **Approach:**
 - Provide analyses and summaries of current infectious disease threats
 - Survey existing forecasts and trends in these threats
 - Analyze and summarize the current situation and trends of these threats in the broader context of the US and world
 - Provide broad overview of other emerging threats

Key Takeaways

Projecting future cases precisely is impossible and unnecessary.

Even without perfect projections, we can confidently draw conclusions:

- Case rates have rebounded slightly higher after prolonged decline and plateau period
- Hospitalization rates remain in slow decline
- Most indicators still point to continued plateaus
- Long term projections that assume a seasonal trend in the winter show impact of vaccine coverage and slow vs. fast evolution of immune escape
 - Broad annual vaccination campaign reduces hospitalizations by 27% over 2 years

Model Updates

- Projected Trajectories from previous rounds remain on target, no new projections made this round

Public Health Emergency Expired

May 11, 2023, marks the end of the federal COVID-19 PHE declaration. After this date, CDC's authorizations to collect certain types of public health data will expire.

- This expiration shifts elements of the COVID-19 pandemic response towards a monitoring and evaluation approach
- Changes data availability and cadence of updates



COVID-19



End of the Federal COVID-19 Public Health Emergency (PHE) Declaration

Updated May 5, 2023 [Español](#) | [Other Languages](#) [Print](#)

OIG's COVID-19 Public Health Emergency Flexibilities End on May 11, 2023 Upon Expiration of the COVID-19 Public Health Emergency Declaration

Important

This notice reminds the health care community that OIG flexibilities, described further below, end upon the expiration of the COVID-19 Declaration on May 11, 2023.

In connection with the [COVID-19 public health emergency declaration](#) (COVID-19 Declaration) first issued by the Secretary of Health and Human Services (HHS) under Section 319 of the Public Health Service Act on January 31, 2020, and subsequently renewed, the Office of Inspector General (OIG) issued two Policy Statements and answered a series of frequently asked questions (FAQs). The Policy Statements and FAQs were designed to provide flexibility and minimize burdens for the health care industry as it faced the challenges of the COVID-19 pandemic. Based on current COVID-19 trends, [HHS plans to let the COVID-19 Declaration expire](#) at the end of the day on May 11, 2023.



U.S. Department of Health and Human Services
Office of Inspector General



Vaccines will remain available.



Access to COVID-19 vaccines will generally not be affected for now. The U.S. government is currently distributing free [COVID-19 vaccines](#) for all adults and children. To help keep communities safe from COVID-19, HHS remains committed to maximizing continued access to COVID-19 vaccines.



COVID-19 at-home tests may not be covered by insurance. Insurance providers will no longer be required to waive costs or provide free COVID-19 tests. CDC's [No Cost COVID-19 Testing Locator](#) can help people find current community and pharmacy partners participating in the [Increasing Community Access to Testing \(ICATT\) program](#).



Treatments will remain available.

Medication to prevent severe COVID-19, [such as Paxlovid](#)  , will remain available for free while supplies last. After that, the price will be determined by the medication manufacturer and your health insurance coverage. Check with your healthcare provider if you need [early treatment to prevent severe COVID-19](#).



National reporting of COVID-19 may change.

We have the right data for this phase of COVID-19 that will allow us to understand what's happening with the virus in America in real-time. Simply put, while what we have going forward will be different, it will still allow CDC, local public health officials, and the members of the public to understand COVID-19 dynamics at the community level.



The following metrics remain available:

COVID-19 hospital admissions.
All hospitals are required to report data through the end of April 2024. This provides a consistent and comprehensive way for weekly tracking of severe COVID-19 at the county level. These data will shift from daily to weekly reporting shortly after May 11.

COVID-19 deaths will remain, but the source of data has changed.
The National Vital Statistics System (NVSS) is the most accurate and complete source of death data, and timeliness of death certificate reporting has improved over the course of the pandemic. A new metric, the percent of deaths that are COVID-19-associated, and other metrics from NVSS will be reported weekly.

Emergency department patient visits with diagnosed COVID-19 will continue to be posted on a weekly basis.
These data cover about three-quarters of the nation's emergency departments and provide information about COVID-19 trends in most states. This is one of the fastest ways to spot changing trends in COVID-19 transmission.

COVID-19 test positivity will remain, but the source of data has changed.
After May 25, CDC will report regional-level test positivity data from the [National Respiratory and Enteric Virus Surveillance System \(NREVS\)](#), a longstanding system with over 450 labs from across the country that voluntarily submit data. These data can provide early indications of COVID-19 transmission.

Wastewater surveillance and genomic surveillance will remain in place.
This will allow the CDC to track transmission and how the virus is mutating.

Count of COVID-19 vaccines administered will remain for jurisdictions who continue to submit data, but frequency will change.
These data will be updated monthly, instead of weekly.




The following data have been removed:

COVID-19 case and death data are no longer highlighted on COVID Data Tracker.

Throughout the pandemic, case and death counts were reported weekly to the CDC by states. Case data has become increasingly unreliable as some states and jurisdictions may no longer collect case data, testing results are sometimes not reported, or some individuals skip testing all together. CDC continues to receive line-level data on COVID-19 cases through the National Notifiable Disease Surveillance System—a system that CDC uses to regularly collect case data for around 120 notifiable diseases. These data are available to the public for analysis at [data.cdc.gov](#).

National, county-level test positivity data from COVID-19 Electronic Reporting (CELR) are no longer available.
This is because after May 11th [laboratories are no longer required to report results](#) .

The V-safe tracking system for health check-ins after vaccination health check-ins is ending.

CDC will continue to monitor COVID-19 vaccines through its other established vaccine safety monitoring systems. V-safe users or others who get vaccinated can report any possible health problems or adverse events following vaccination to the [Vaccine Adverse Event Reporting System](#) .



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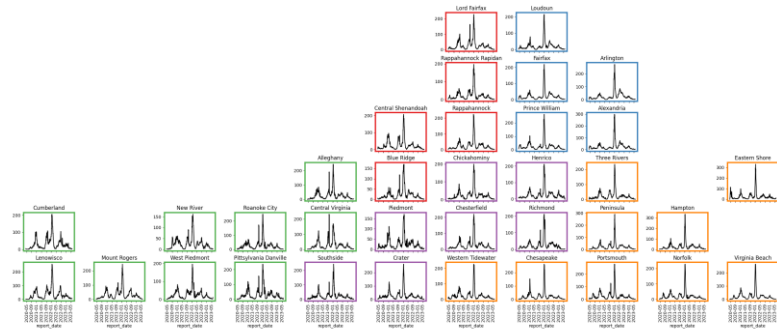
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9-Jun-23

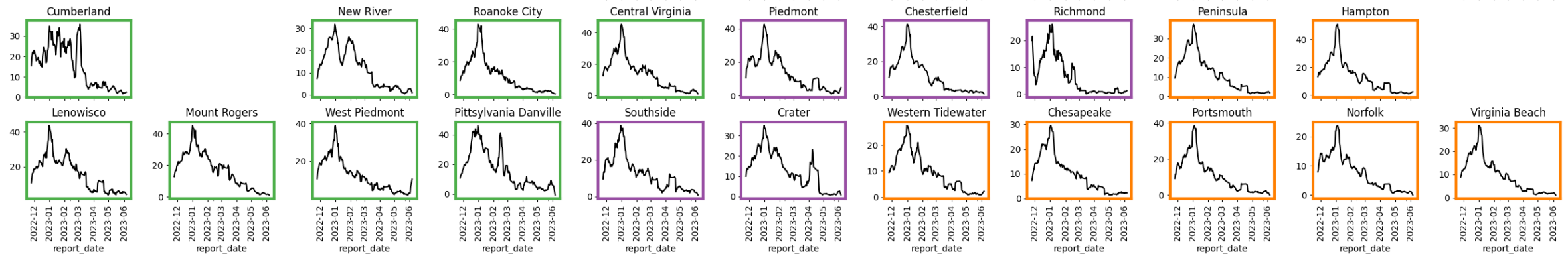
[CDC Announcement](#)

COVID-19 Surveillance

Case Rates (per 100k)



Whole pandemic

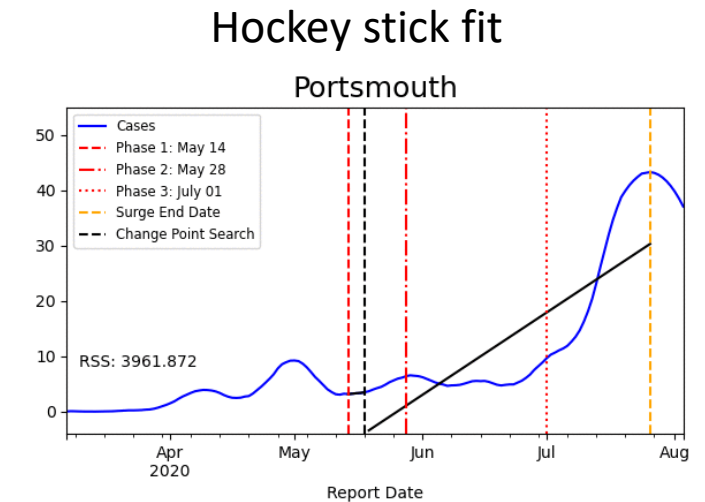


Since December 2021

District Trajectories

Goal: Define epochs of a Health District's COVID-19 incidence to characterize the current trajectory

Method: Find recent peak and use hockey stick fit to find inflection point afterwards, then use this period's slope to define the trajectory

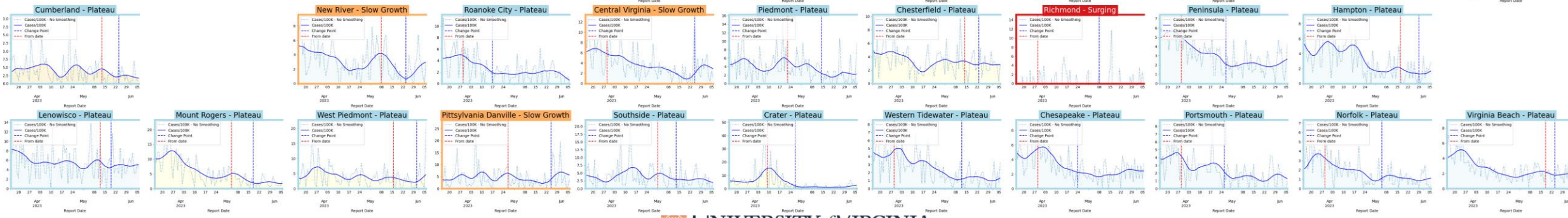
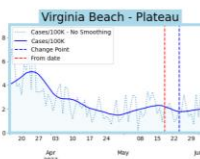
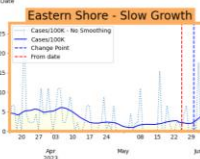
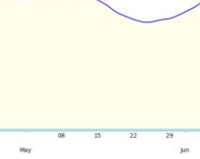
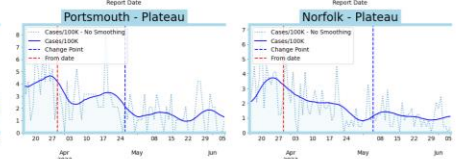
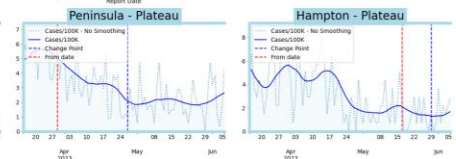
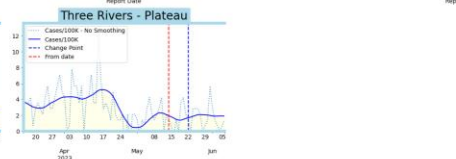
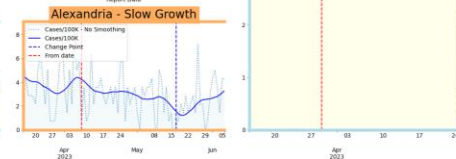
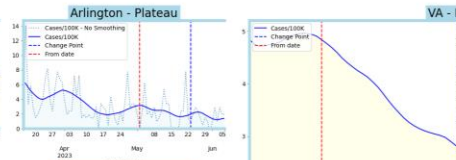
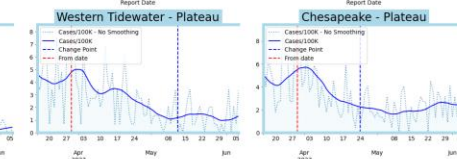
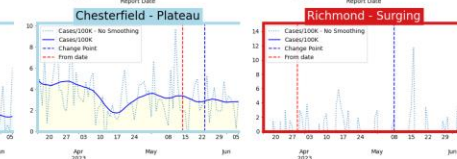
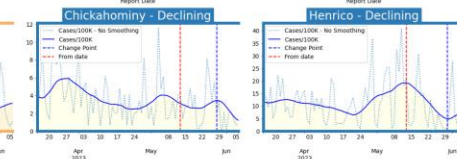
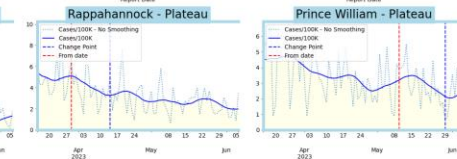
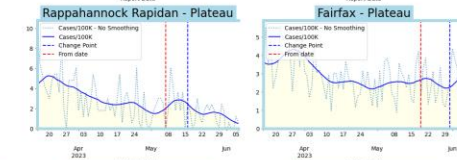
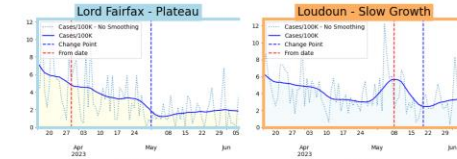
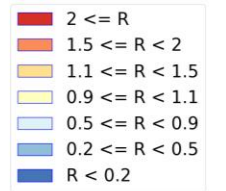


Trajectory	Description	Weekly Case Rate Slope (per 100k)	Weekly Hosp Rate Slope (per 100k)
Declining	Sustained decreases following a recent peak	slope < -0.88/day	slope < -0.07/day
Plateau	Steady level with minimal trend up or down	-0.88/day < slope < 0.42/day	-0.07/day < slope < 0.07/day
Slow Growth	Sustained growth not rapid enough to be considered a Surge	0.42/day < slope < 2.45/day	0.07/day < slope < 0.21/day
In Surge	Currently experiencing sustained rapid and significant growth	2.45/day < slope	0.21/day < slope

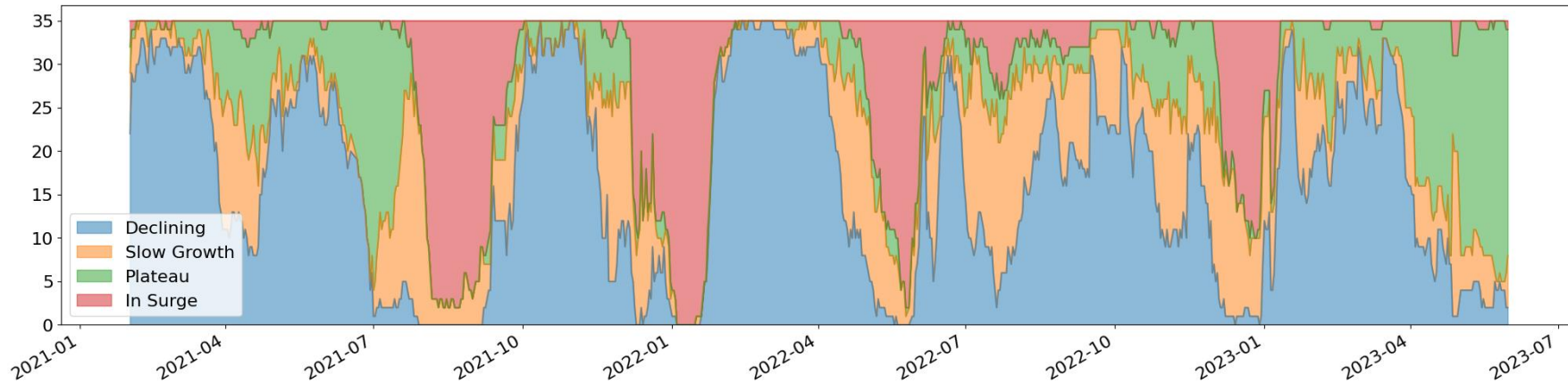
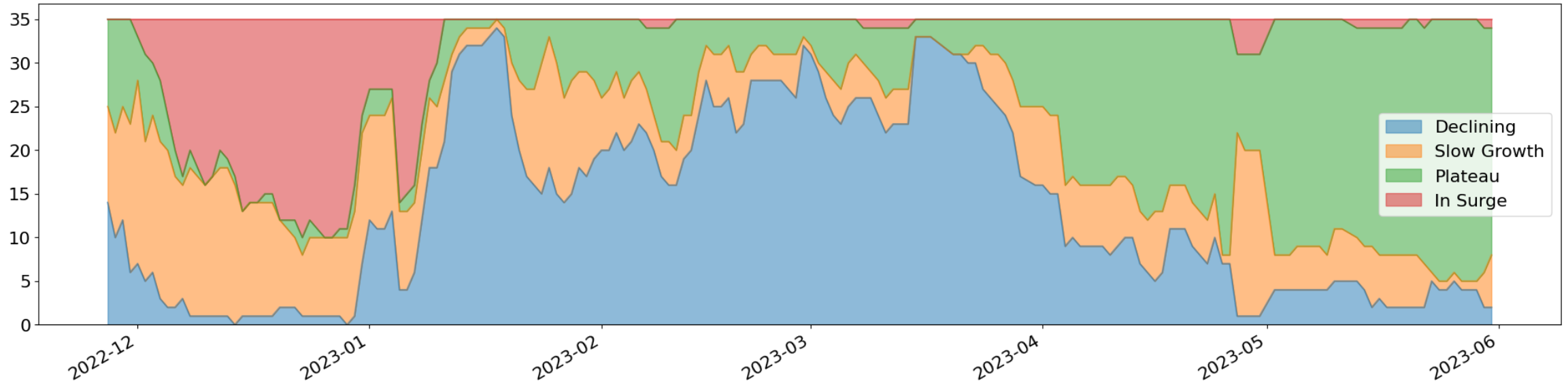
District Case Trajectories – last 10 weeks

Status	Number of Districts	
	Current Week	Last Week
Declining	2	(2)
Plateau	25	(26)
Slow Growth	7	(6)
In Surge	1	(1)

Curve shows smoothed case rate (per 100K)
Trajectories of states in label & chart box
Case Rate curve colored by Reproductive
number



District Case Trajectories – Recent 6 months



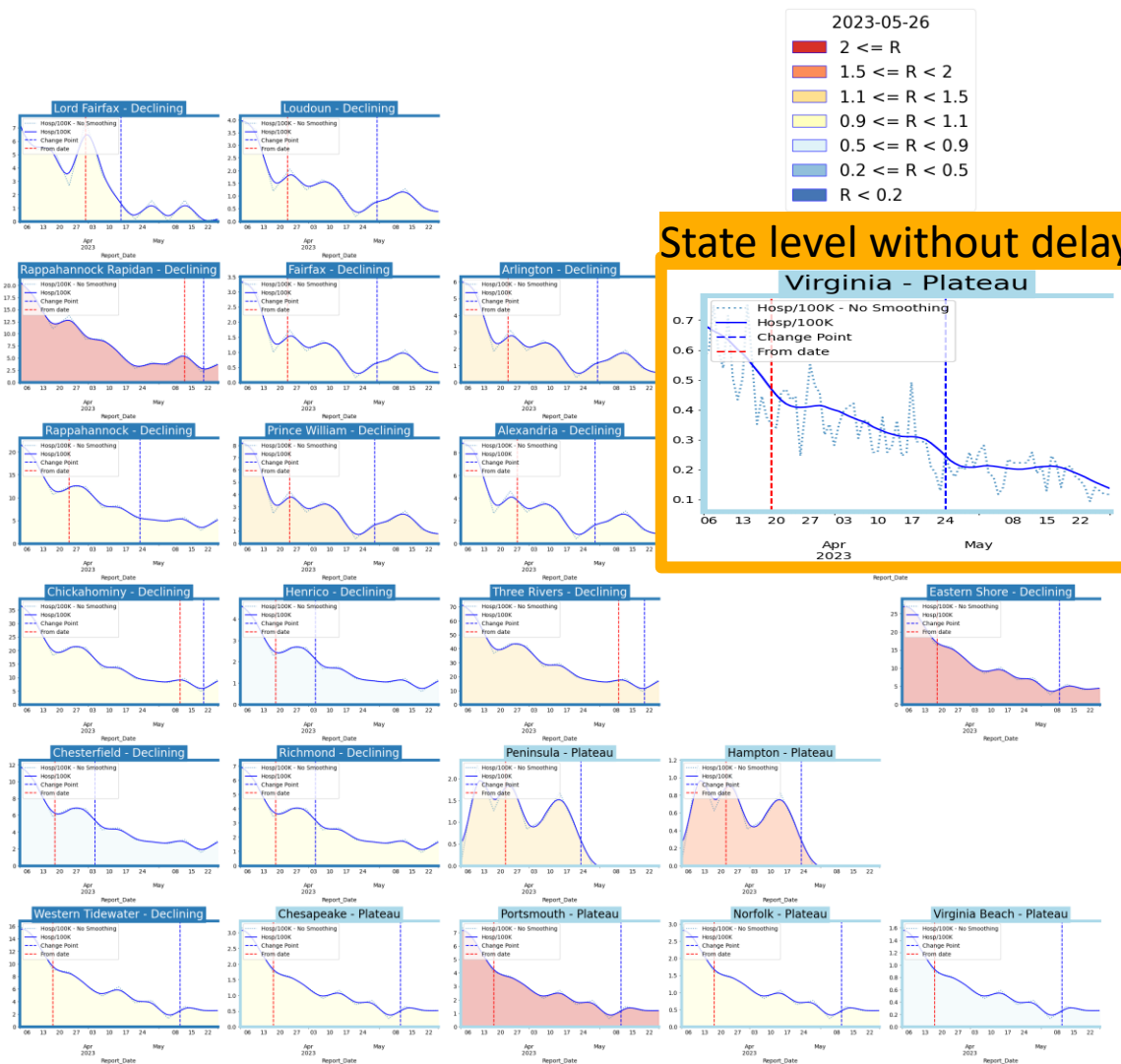
District Hospital Trajectories – last 10 weeks

Status	Number of Districts	
	Current Week	Last Week
Declining	29	(8)
Plateau	6	(27)
Slow Growth	0	(0)
In Surge	0	(0)

Hospitalization by county is delayed, these data are current as week ending of **May 29th**

May 29th

Curve shows smoothed hospitalization rate
(per 100K) by district
Hosp rate curve colored by R_e number



COVID-19 Growth Metrics

Estimating Daily Reproductive Number – VDH report dates

June 6th Estimates

Region	Date Confirmed R_e	Date Confirmed Diff Last Week
State-wide cases	1.078	0.080
State-wide hosps	0.987	0.024
Central	1.202	0.320
Eastern	1.075	0.065
Far SW	0.928	-0.164
Near SW	1.042	-0.227
Northern	1.075	0.124
Northwest	1.086	0.078

Methodology:

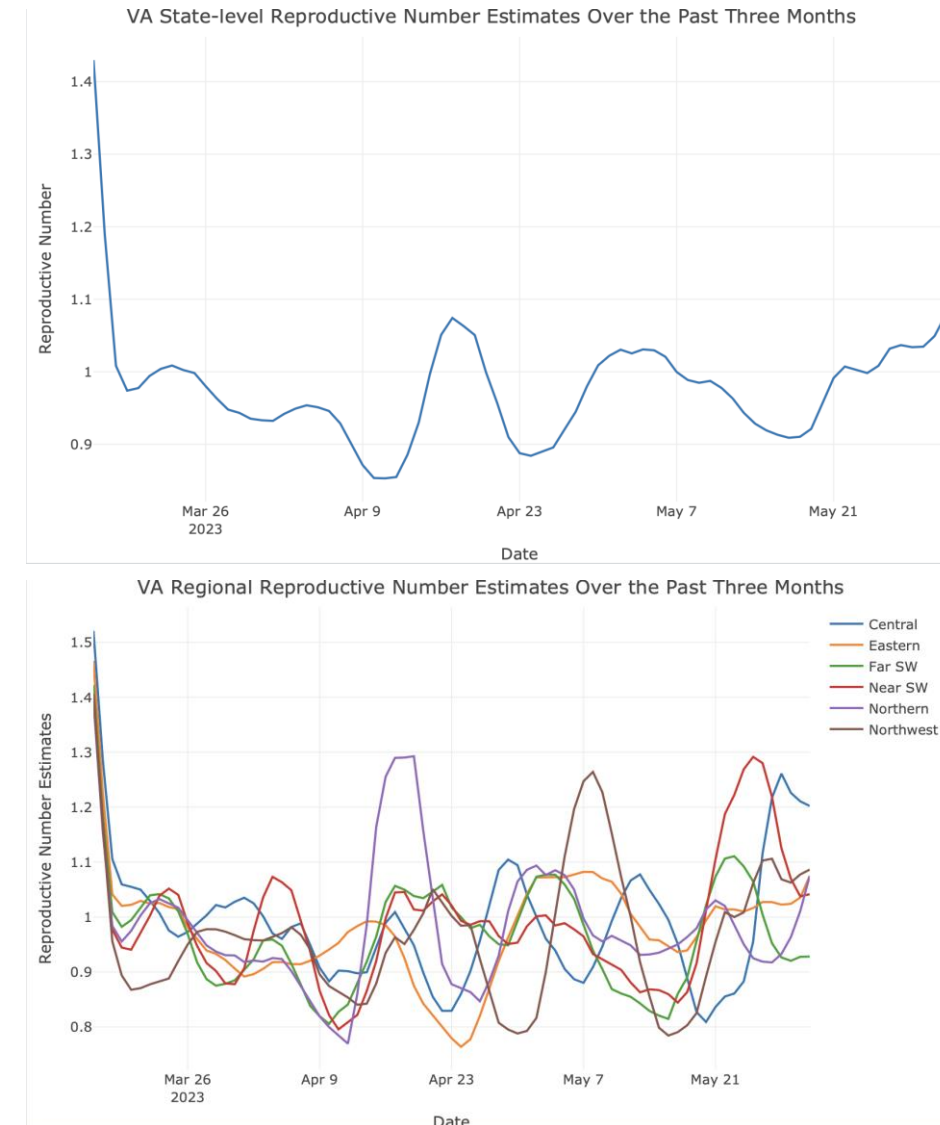
Wallinga-Teunis method (Epi-Estim) for cases by confirmation date.

Cori, A., Ferguson, N. M., Fraser, C., & Cauchemez, S. (2013). A new framework and software to estimate time-varying reproduction numbers during epidemics. *American journal of epidemiology*, 178(9), 1505-1512.

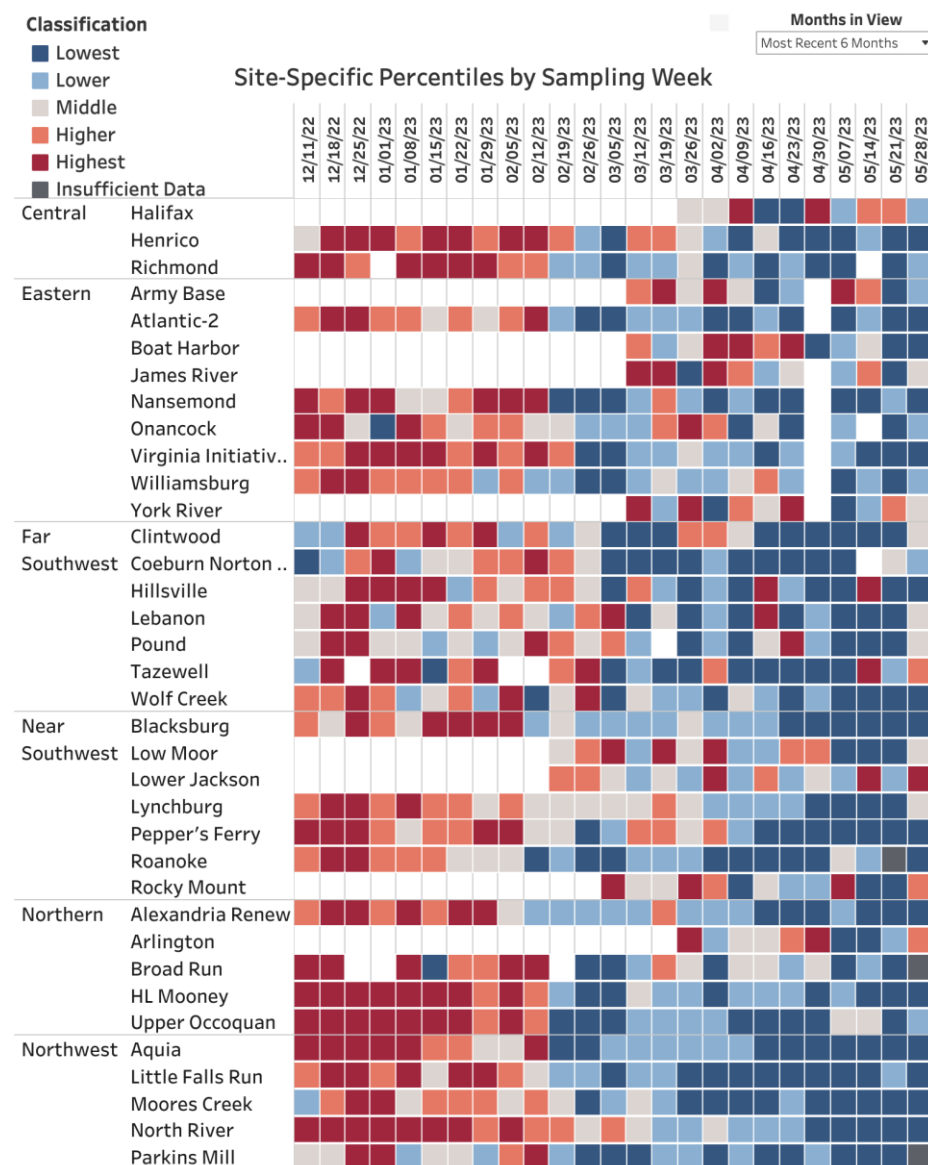
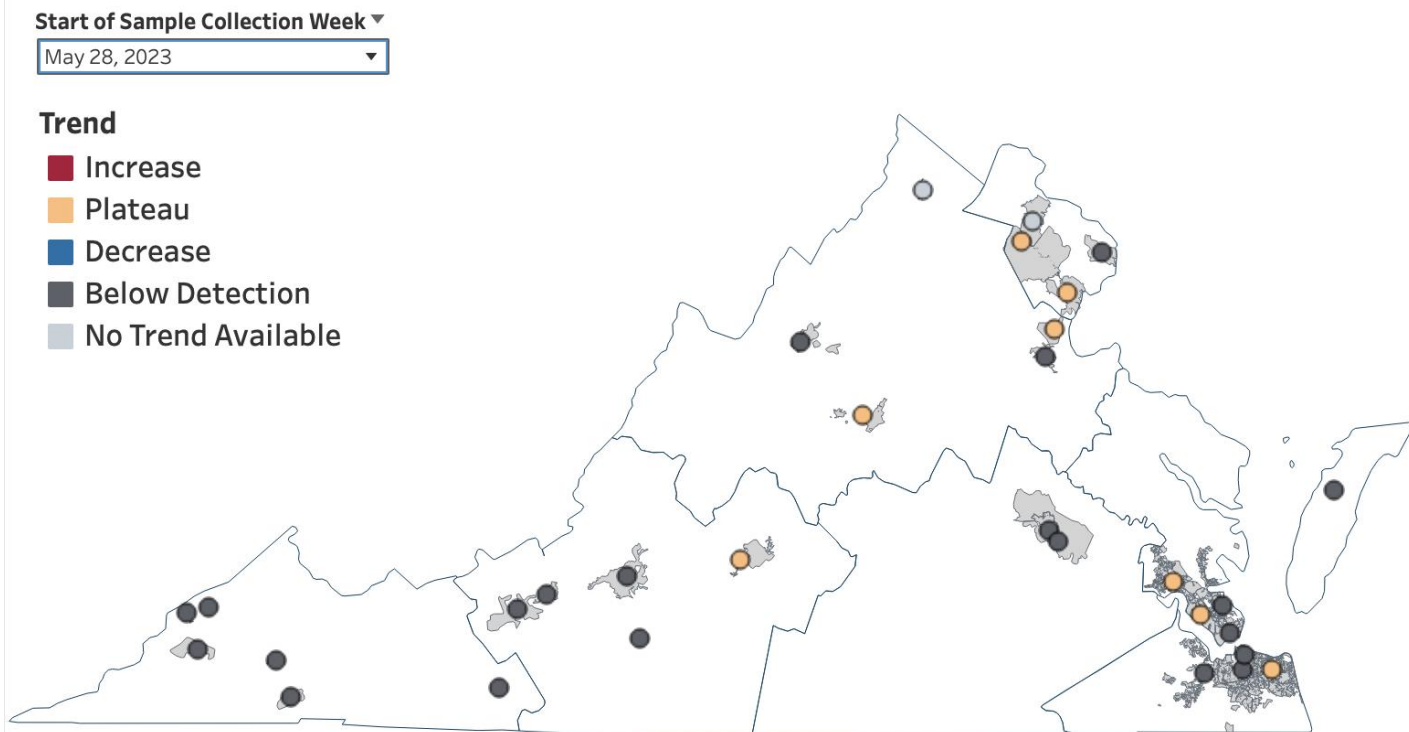
Serial interval used: mean = 3.19, standard deviation= 0.122

Xu, X., Wu, Y., Kummer, A. G., Zhao, Y., Hu, Z., Wang, Y., ... & Yu, H. (2023). Assessing changes in incubation period, serial interval, and generation time of SARS-CoV-2 variants of concern: a systematic review and meta-analysis. *medRxiv*, 2023-05.

Data was interpolated then smoothed (using 7 day rolling mean) to account for missing data.

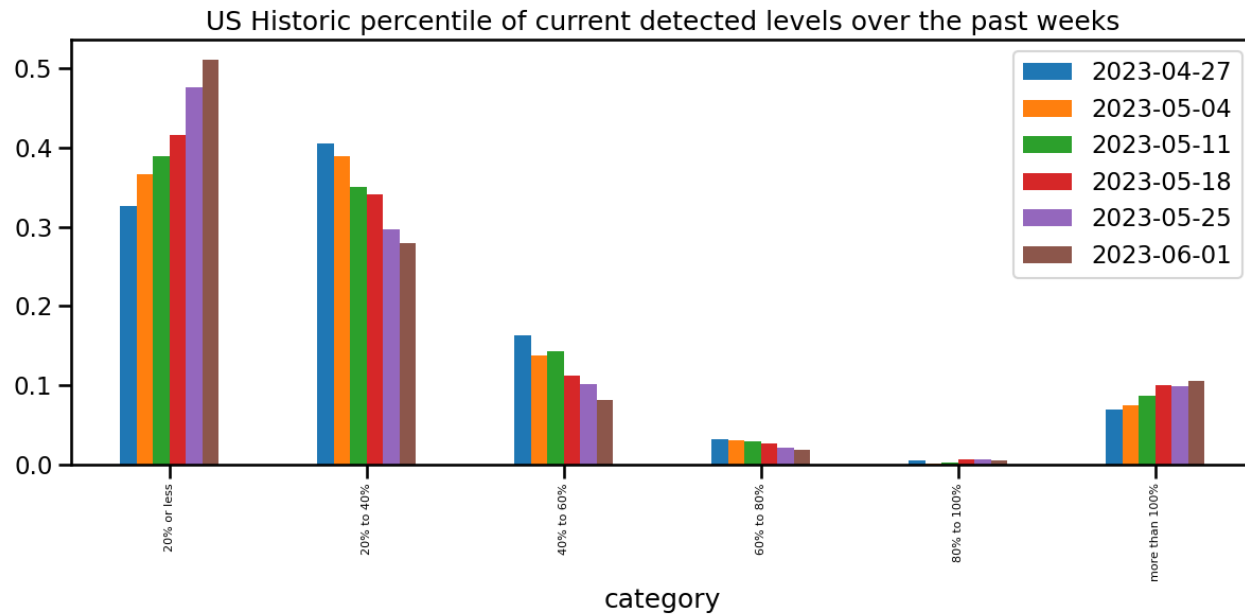


VA Wastewater Data Update

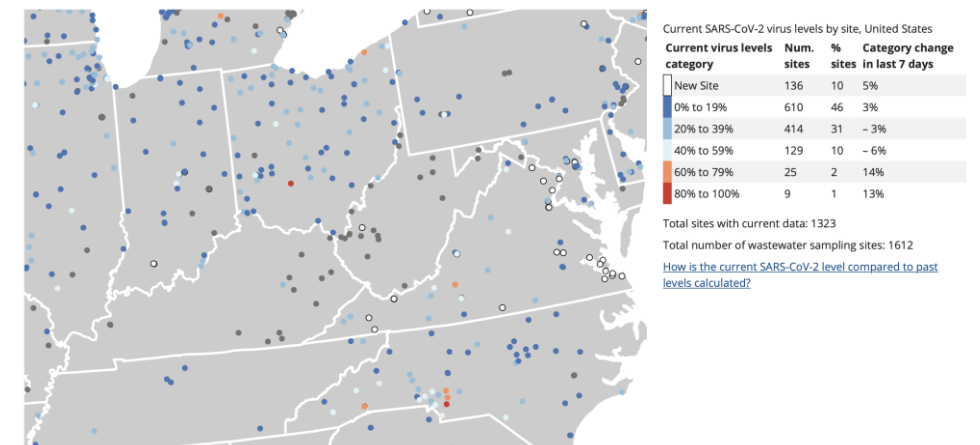
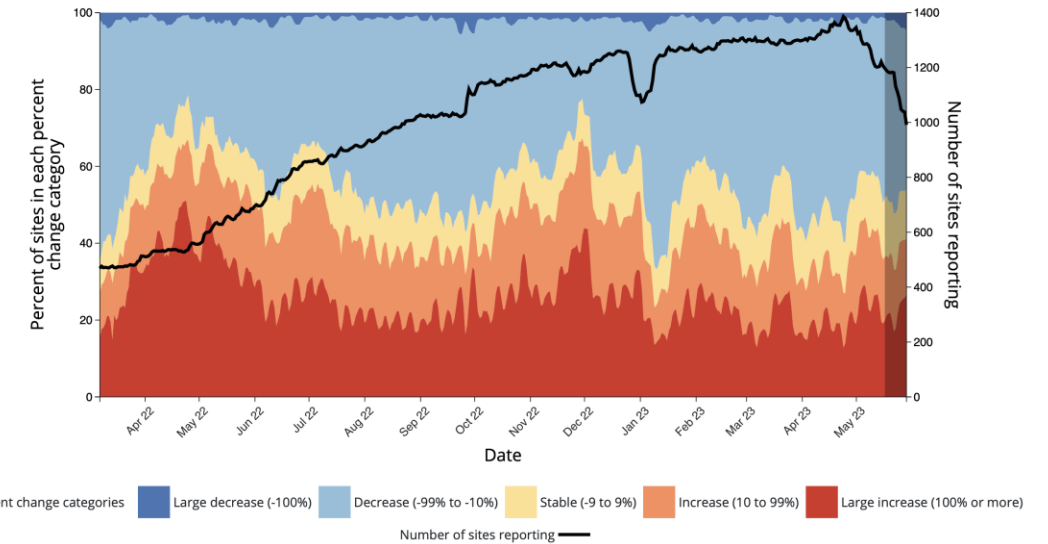


US Wastewater Monitoring

Wastewater provides a coarse estimate of COVID-19 levels in communities and can be a good indicator of activity levels



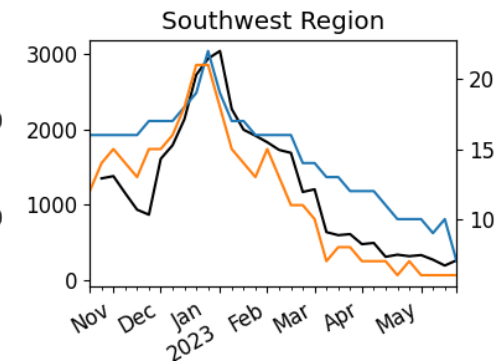
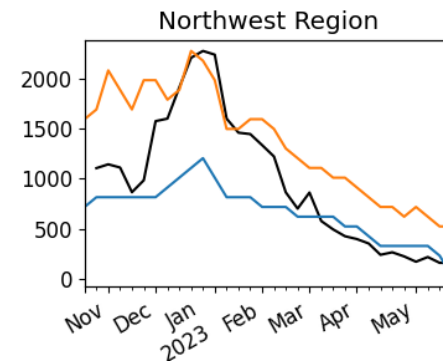
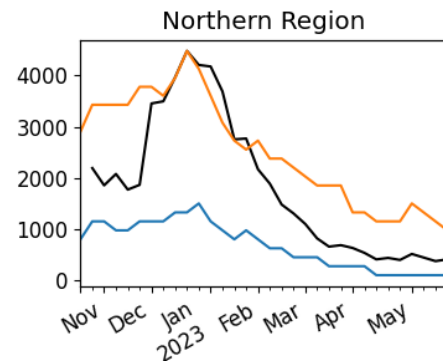
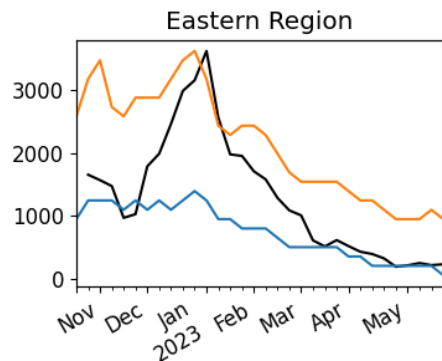
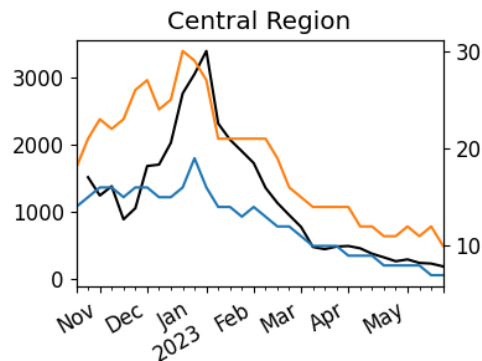
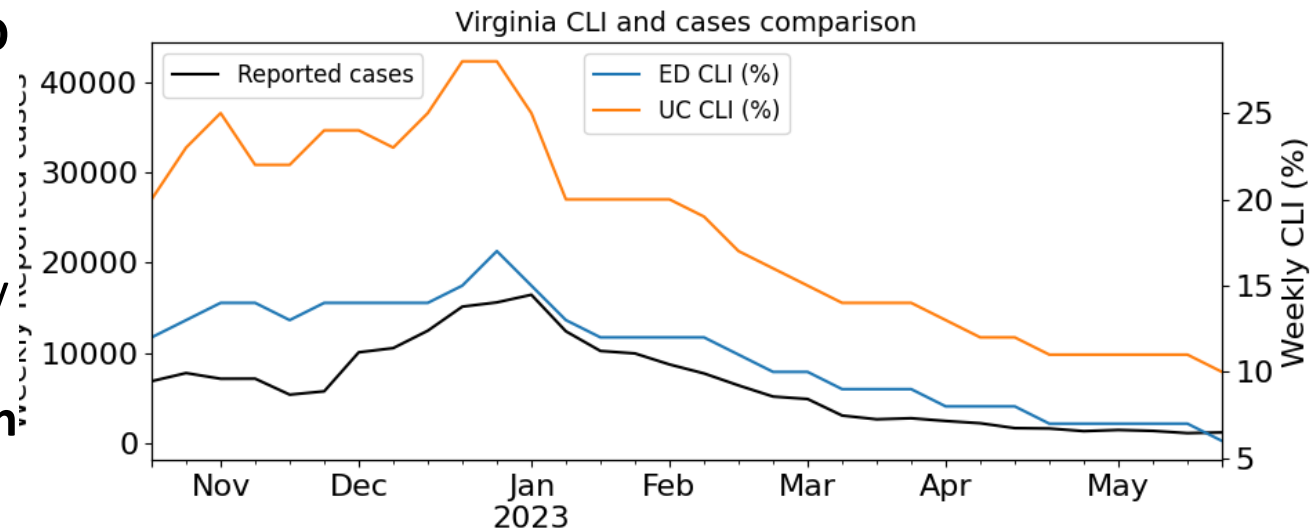
Percent of sites in each percent change category over time, United States*



COVID-like Illness Activity

COVID-like Illness (CLI) gives a measure of COVID transmission in the community

- Emergency Dept (ED) based CLI is more correlated with case reporting
- Urgent Care (UC) is a leading indicator but may be influenced by testing for other URIs
- **Levels continue to decline into lowest levels in past 8 months**



COVID-19 Severity Metrics

Hospitalizations in VA by Age

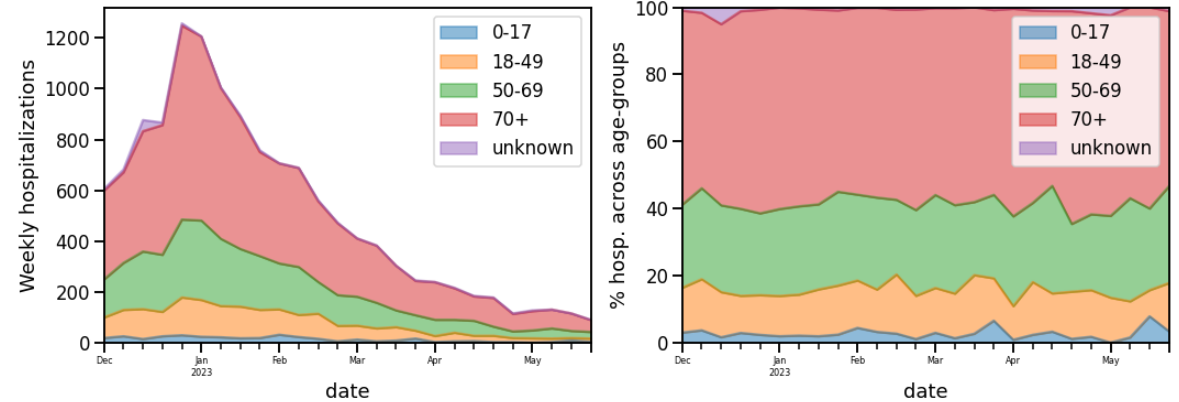
Age distribution in hospitals relatively stable

- Uptick in hospitalizations mostly fueled by 70+ age group
- Pediatric hospitalizations level off after uptick last week

Note: These data are lagged and based on HHS hospital reporting

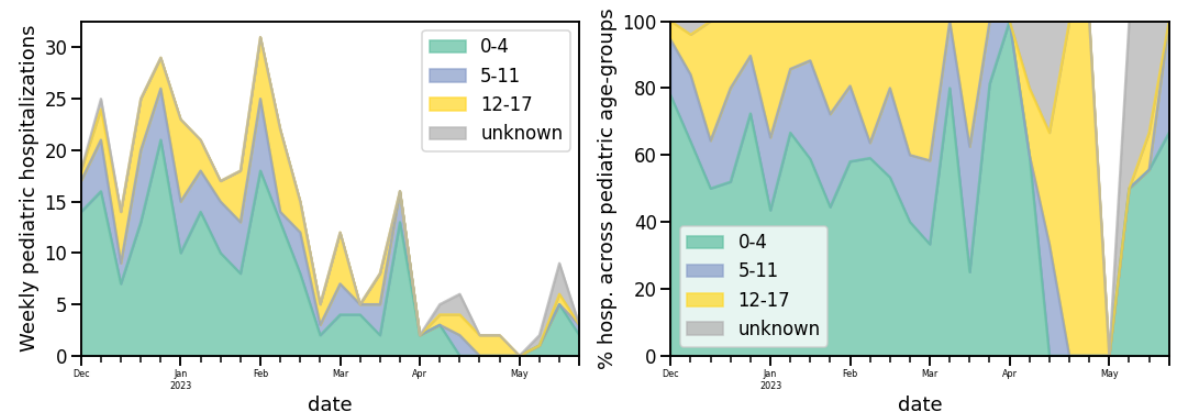
Virginia Hospitalizations by Age (all ages)

Hospitalizations - VA



Pediatric Hospitalizations by Age (0-17yo)

Pediatric hospitalizations - VA



COVID-19 Spatial Epidemiology

ZIP Code level fortnightly case rate (per 100K)

New cases per 100k in the last fortnight by ZIP code

- Statewide COVID19 case rates remain at near historic lows.
- Nassawadox is reporting an unusually high case rate. If accurate, it is five times higher than the top ZIP Code at last report.
- Burkeville is the only ZIP Code with a state prison currently in the top 10.
- Areas with high case rates are sporadic; with slight clustering in Far SW and Southside.

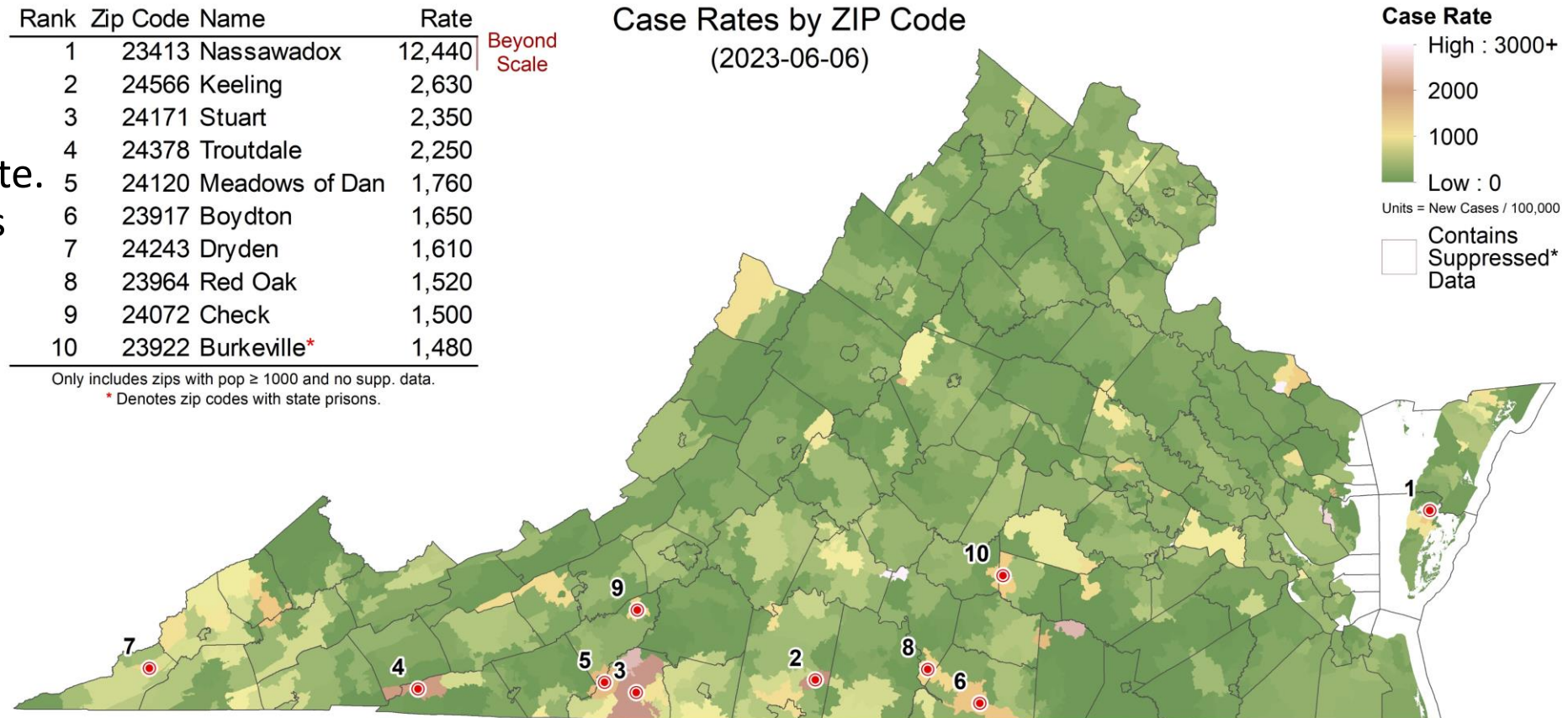
Rank	Zip Code	Name	Rate
1	23413	Nassawadox	12,440
2	24566	Keeling	2,630
3	24171	Stuart	2,350
4	24378	Troutdale	2,250
5	24120	Meadows of Dan	1,760
6	23917	Boydton	1,650
7	24243	Dryden	1,610
8	23964	Red Oak	1,520
9	24072	Check	1,500
10	23922	Burkeville*	1,480

Only includes zips with pop ≥ 1000 and no supp. data.

* Denotes zip codes with state prisons.

Beyond
Scale

Case Rates by ZIP Code
(2023-06-06)

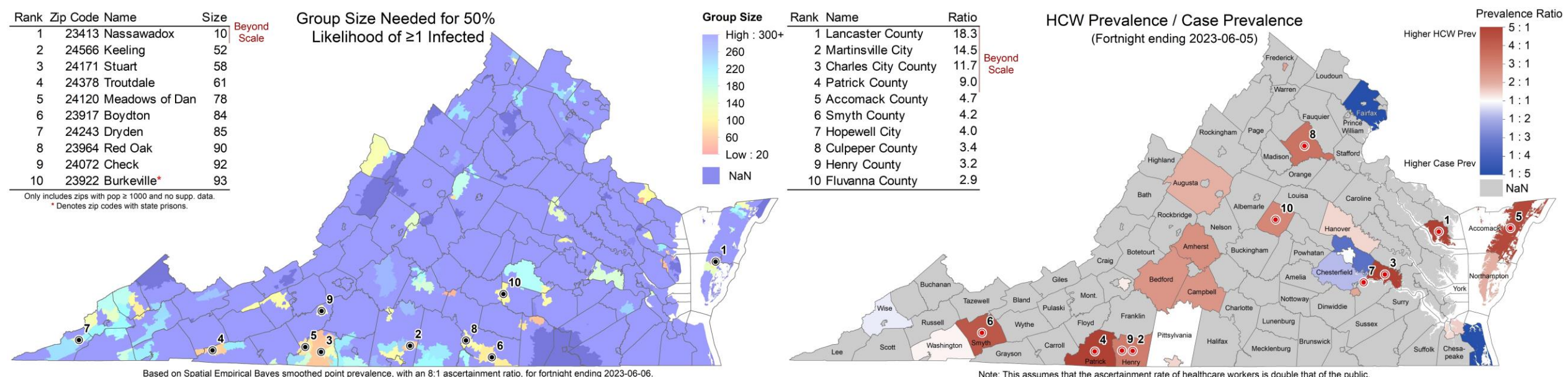


Based on Spatial Empirical Bayes smoothed point prevalence, with an 8:1 ascertainment ratio, for fortnight ending 2023-06-06.

Risk of Exposure by Group Size and HCW prevalence

Case prevalence in the last **fortnight** by zip code used to calculate risk of encountering someone infected in a gathering of randomly selected people

- **Group Size:** Assumes **8 undetected infections** per confirmed case (ascertainment rate from recent seroprevalence survey) and shows minimum size of a group with a 50% chance an individual is infected by zip code (e.g., in a group of 10 in Nassawadox, there is a 50% chance someone will be infected).
- **HCW ratio:** Case rate among health care workers (HCW) in the last fortnight using patient facing health care workers as the numerator / population's case prevalence. Again, high HCW ratios are found in Southwest.



Current Hot-Spots

Case rates that are significantly different from neighboring areas or model projections

- **Spatial:** Getis-Ord Gi* based hot spots compare clusters of zip codes with **fortnightly** case prevalence higher than nearby zip codes to identify larger areas with statistically significant deviations
- **Temporal:** The fortnightly case rate (per 100K) projected in March compared to those observed by county, which highlights temporal fluctuations that differ from the model's projections.
- Low prevalence rates result in sporadic spatial hotspots. Model overpredictions seen in Southside, and to a lesser extent New River and Crater. Pitt-Dan and Lenowisco saw slightly more cases than models expected.

Spatial Hotspots

Spot	Zip Code	Name	Conf.
1	23413	Nassawadox	99%
2	24171	Stuart	99%
3	24566	Keeling	95%

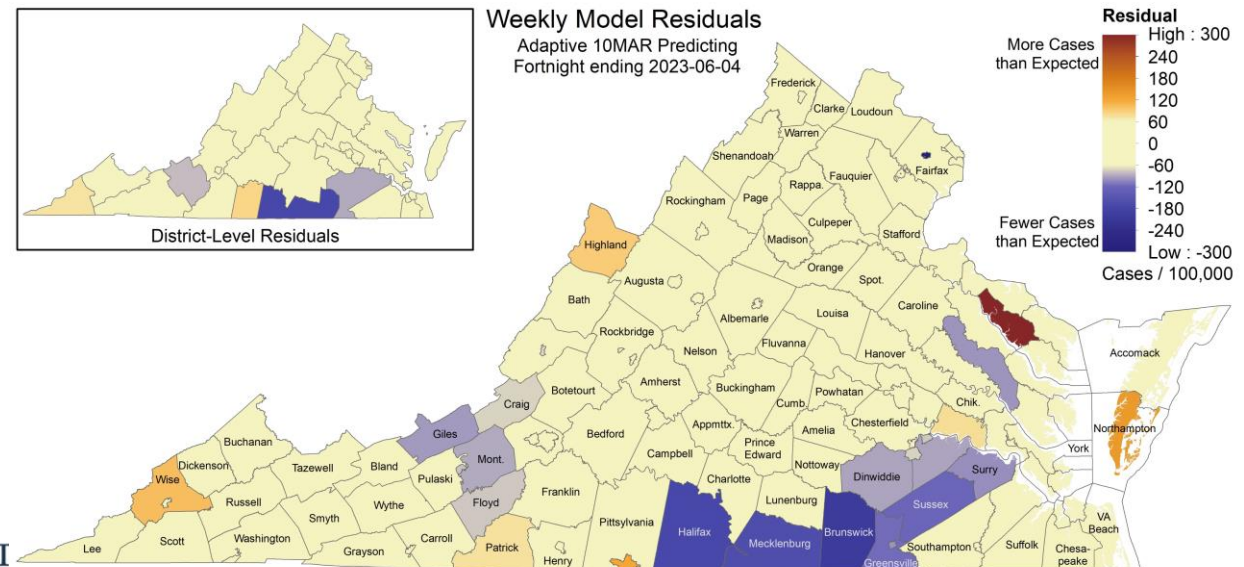
* Denotes zip codes with state prisons.

Point Prevalence Hot Spots by Zip Code



Based on Global Empirical Bayes smoothed point prevalence for fortnight ending 2023-06-06.

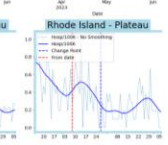
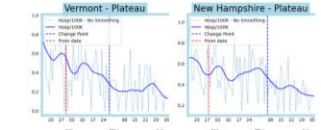
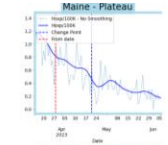
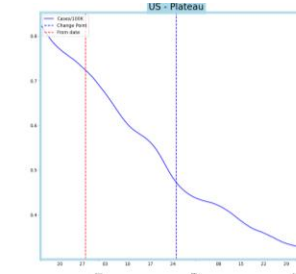
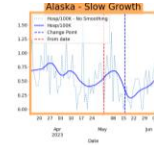
Clustered Temporal Hotspots



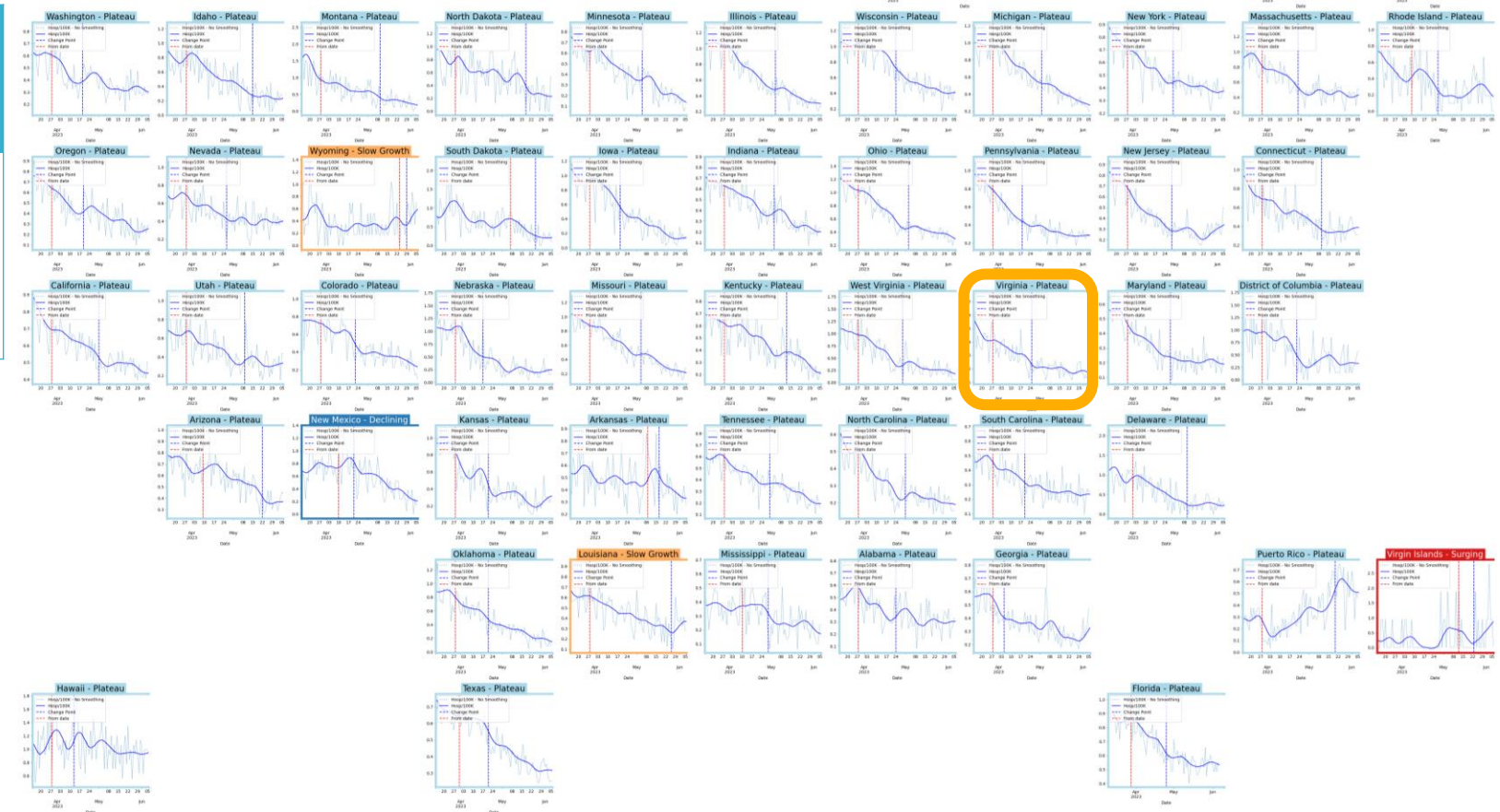
Health District Level Moran's I = 0.022057, Z-Score = 0.927616, P-Value = 0.353607
No Residual Autocorrelation Detected

COVID-19 Broader Context

United States Hospitalizations



Status	Current Week	Last Fortnight
Declining	1	(11)
Plateau	48	(41)
Slow Growth	3	(1)
In Surge	1	(0)

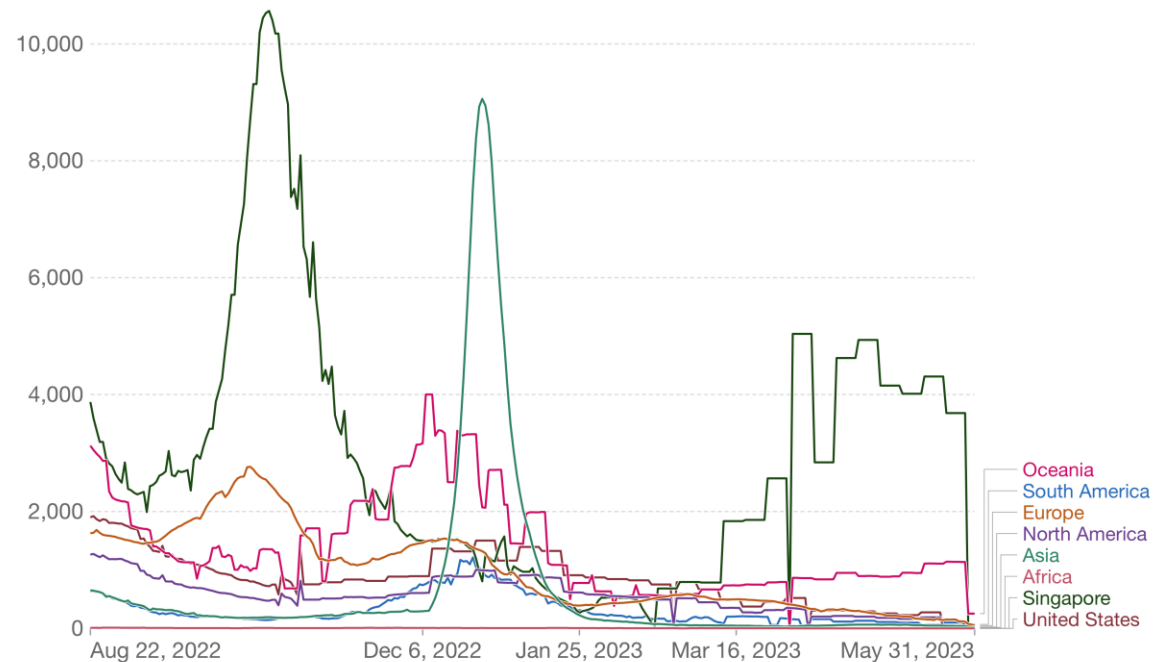


Around the World – Various trajectories

Confirmed cases

Weekly confirmed COVID-19 cases per million people

Weekly confirmed cases refer to the cumulative number of confirmed cases over the previous week.



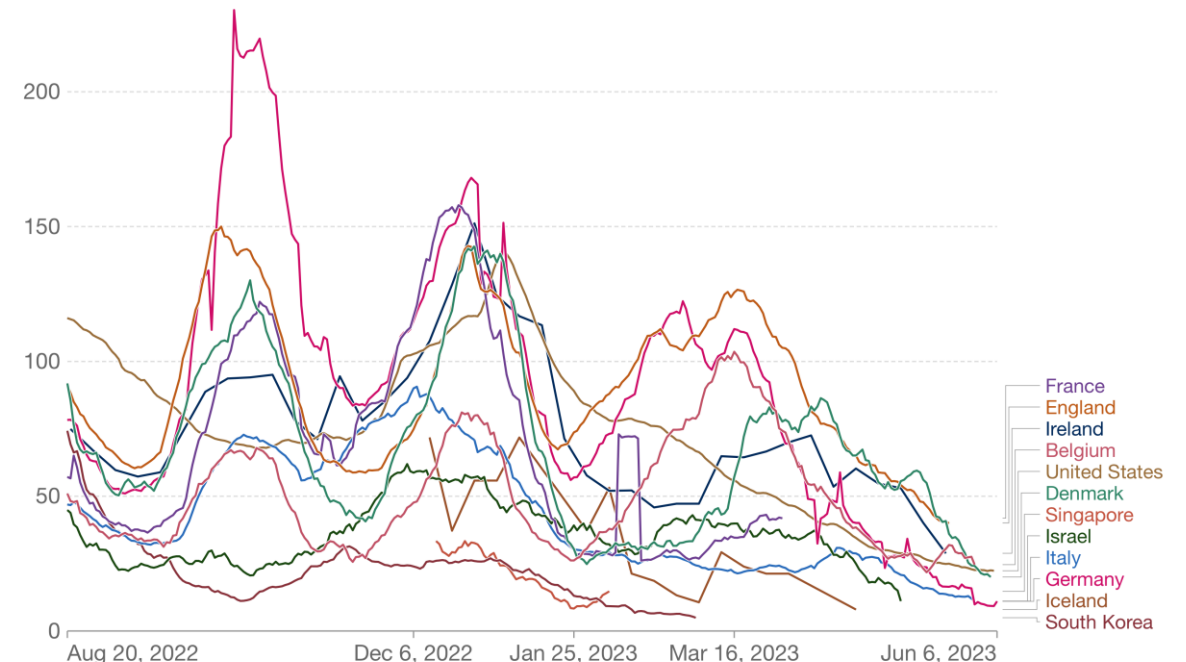
Source: WHO COVID-19 Dashboard

CC BY

Hospitalizations

Weekly new hospital admissions for COVID-19 per million people

Weekly admissions refer to the cumulative number of new admissions over the previous week.



Source: Official data collated by Our World in Data

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COVID-19 Genomic Update

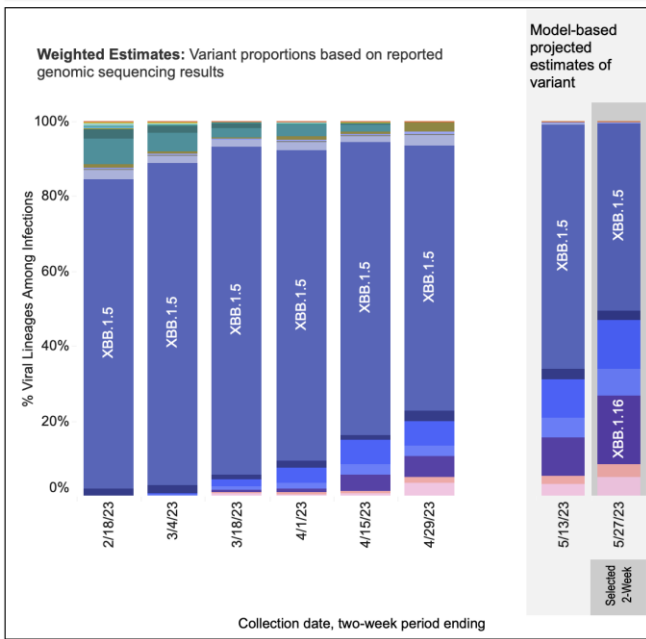
SARS-CoV2 Variants of Concern

Emerging variants have potential to continue to alter the future trajectories of pandemic and have implications for future control

- **Variants have been observed to:** increase transmissibility, increase severity (more hospitalizations and/or deaths), and limit immunity provided by prior infection and vaccinations

Weighted and Nowcast Estimates in HHS Region 3 for 2-Week Periods in 2/5/2023 – 5/27/2023

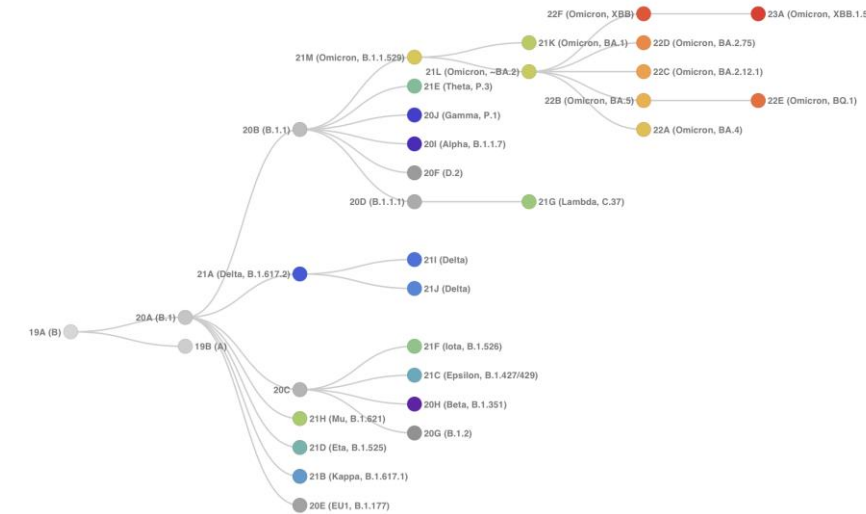
Hover over (or tap in mobile) any lineage of interest to see the amount of uncertainty in that lineage's estimate.



Nowcast Estimates in HHS Region 3 for 5/14/2023 – 5/27/2023

Region 3 - Delaware, District of Columbia, Maryland, Pennsylvania, Virginia, and West Virginia

WHO label	Lineage #	US Class	%Total	95%PI	
Omicron	XBB.1.5	VOC	50.1%	43.1-57.0%	
	XBB.1.16	VOC	18.4%	12.1-26.9%	
	XBB.1.9.1	VOC	13.0%	10.0-16.6%	
	XBB.1.9.2	VOC	7.3%	5.1-10.3%	
	XBB.2.3	VOC	4.9%	2.7-8.6%	
	XBB.1.16.1	VOC	3.4%	1.9-5.9%	
	XBB.1.5.1	VOC	2.5%	1.7-3.7%	
	XBB	VOC	0.3%	0.1-0.5%	
	CH.1.1	VOC	0.1%	0.1-0.2%	
	FD.2	VOC	0.1%	0.0-0.1%	
	BQ.1.1	VOC	0.0%	0.0-0.0%	
	BQ.1	VOC	0.0%	0.0-0.0%	
	BA.5	VOC	0.0%	0.0-0.0%	
	BN.1	VOC	0.0%	0.0-0.0%	
Other	BA.2	VOC	0.0%	0.0-0.0%	
	BA.5.2.6	VOC	0.0%	0.0-0.0%	
	Other*		0.0%	0.0-0.0%	



<https://clades.nextstrain.org>

Omicron Updates*

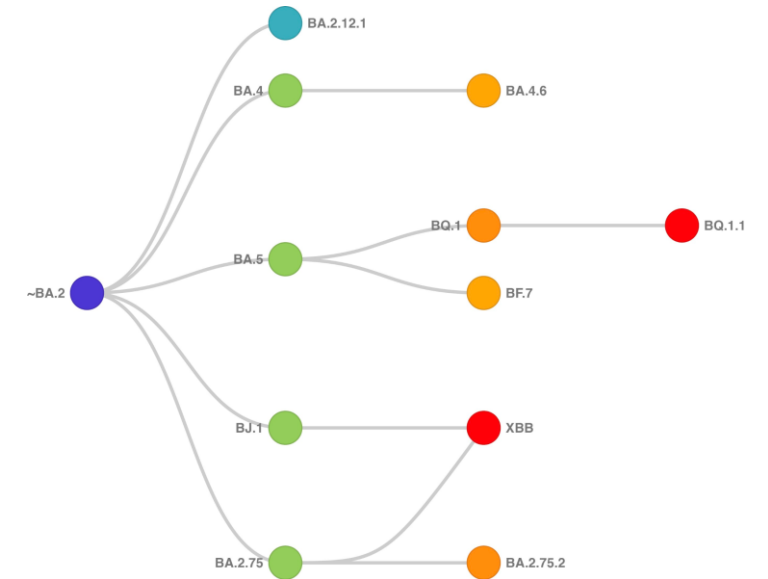
- XBB.1.5 proportions have fallen to 50% from 60%
- XBB.1.16 remains flat at 18% with XBB.1.16.1 at 3%
- XBB.1.9.1 now at 13% (XBB.1.9.X combined was 13%)
- XBB.1.9.2 now at 7% last week
- XBB.1.5.1 steady at ~3%
- XBB.2.3 now at 5% up from 3% last week

*percentages are CDC NowCast Estimates

SARS-CoV2 Sequencing

Emerging variants have potential to continue to alter the future trajectories of pandemic and have implications for future control

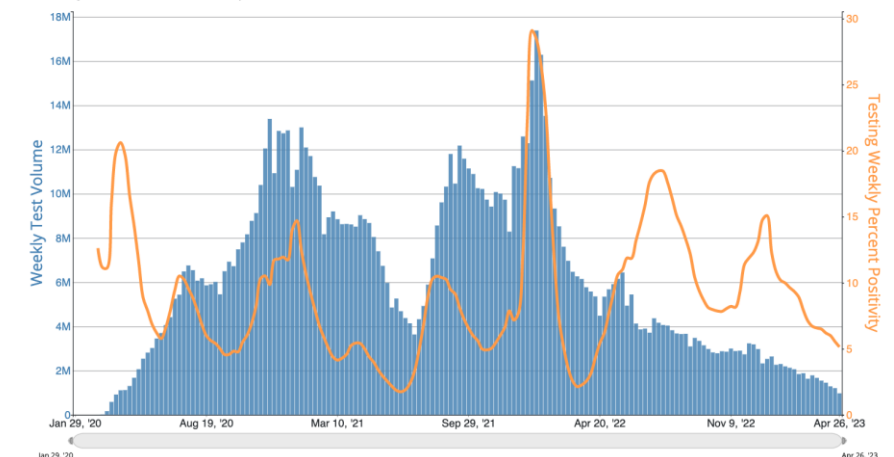
- Current proportion of cases being sequenced is on a downward trend nationally.
- Leveraging additional resources such as wastewater sequencing and adopting into existing infrastructure will be an important supplement



<https://clades.nextstrain.org>

United States

Weekly Nucleic Acid Amplification Tests (NAATs) Performed and COVID-19 Nucleic Acid Amplification Tests (NAATs) 7-day Percent Positivity in The United States Reported to CDC



https://covid.cdc.gov/covid-data-tracker/#trends_7daytestresultsreported_7daytestingpositive_00

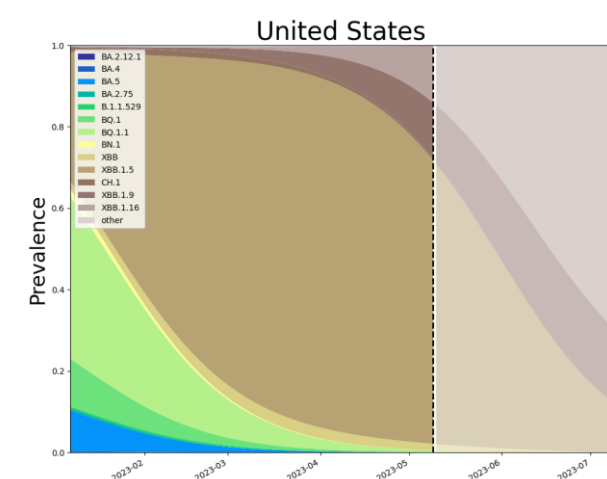
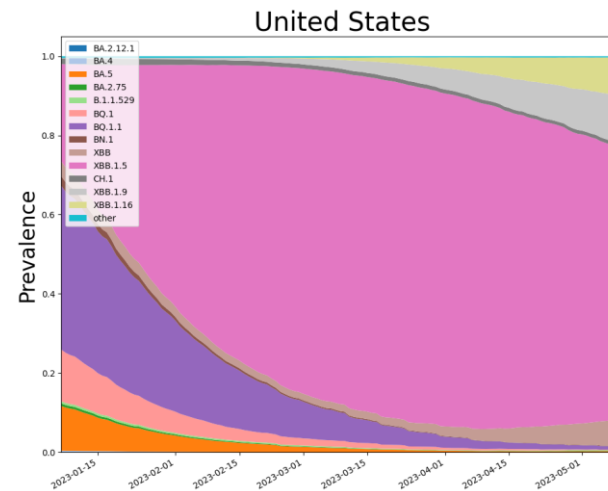
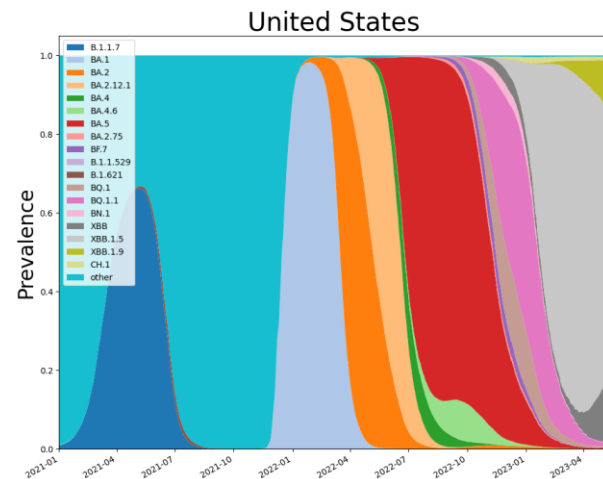
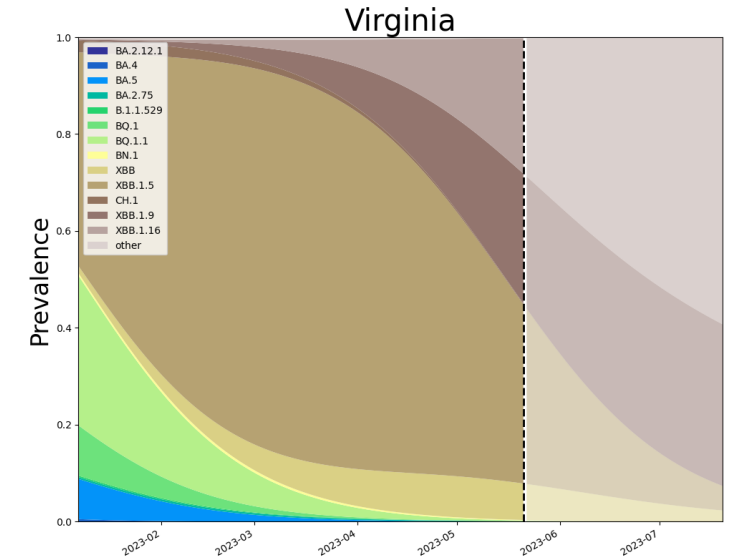
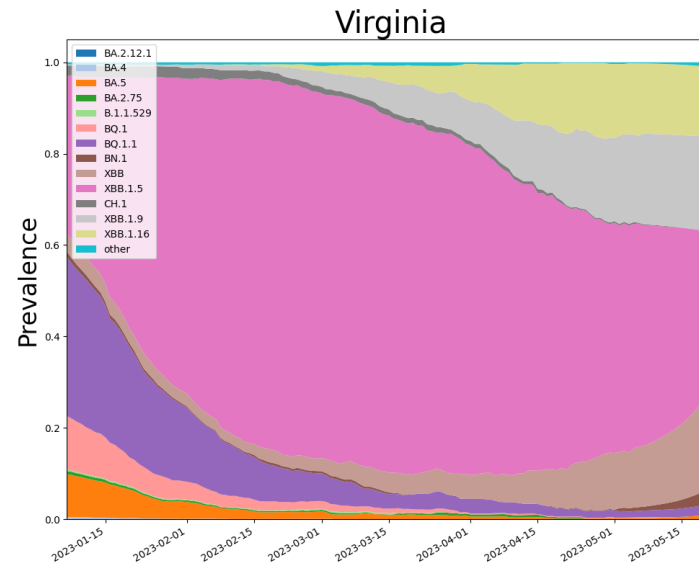
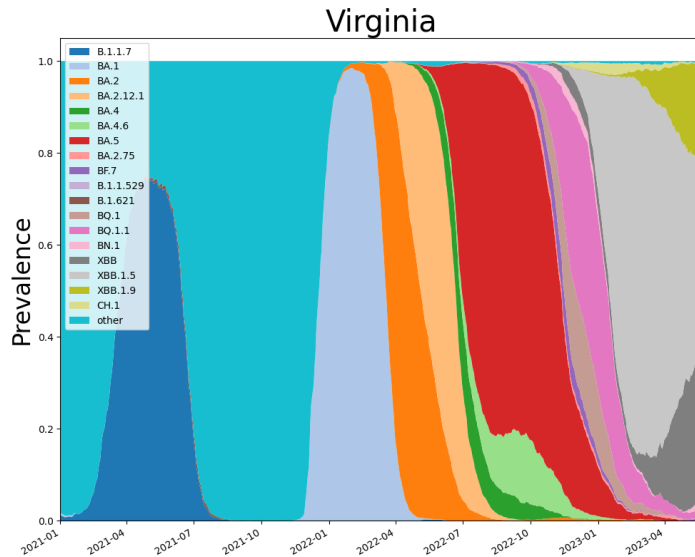
SARS-CoV2 Omicron Sub-Variants

covSPECTRUM

Enabled by data from GISAID

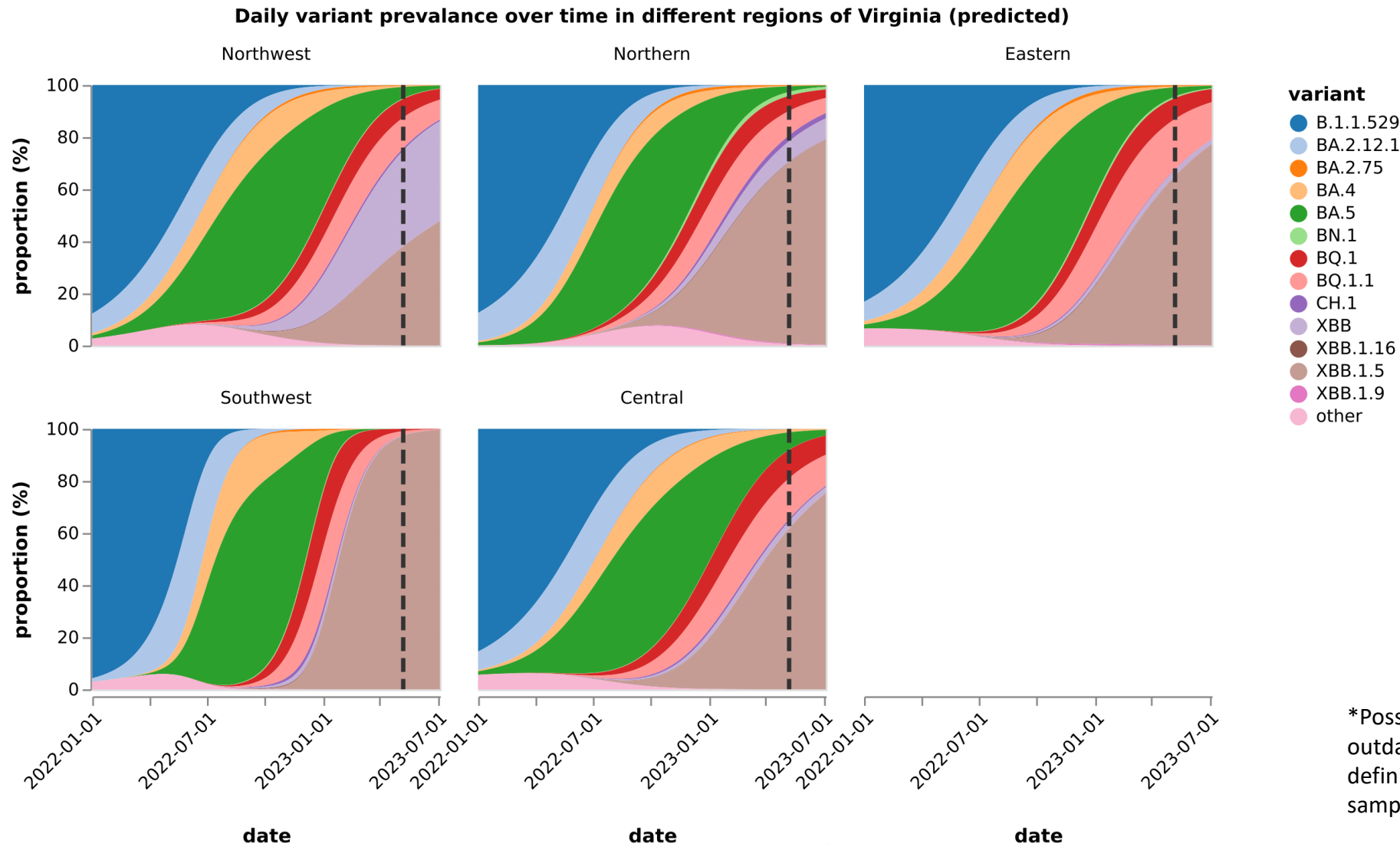
As detected in whole Genomes in public repositories

VoC Polynomial Fit Projections



Note:
Everything
from dotted
line forward is
a projection.

SARS-CoV2 Omicron Sub-Variants



*Possibly impacted by outdated pangolin definitions and low sample numbers

SARS-CoV2 Omicron Sub-Variants

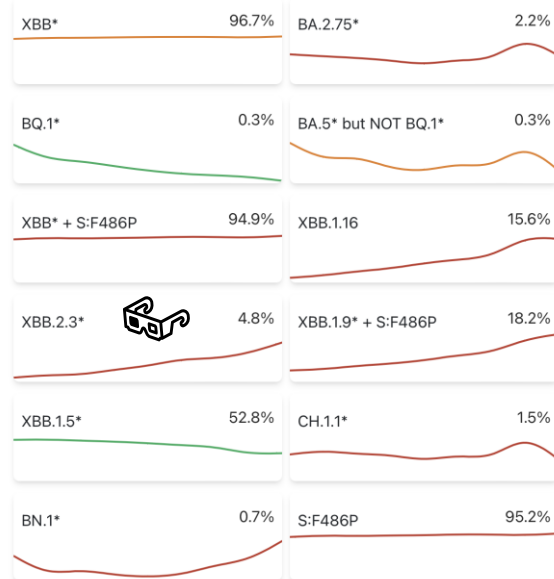
COV-spectrum

“Editor’s choice”
Variants to watch

Known variants

Which variant would you like to explore?

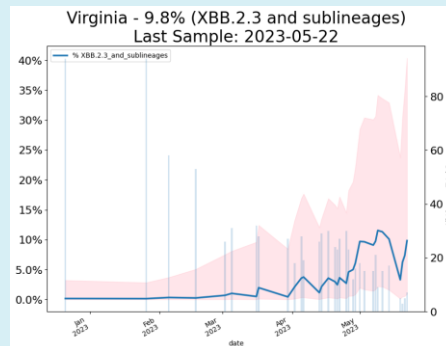
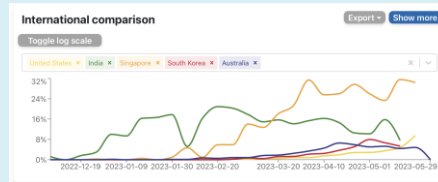
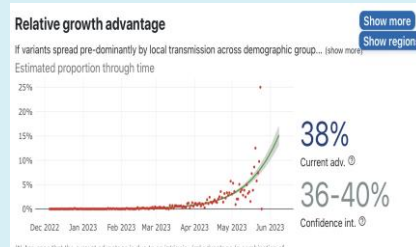
Editor's choice ▼



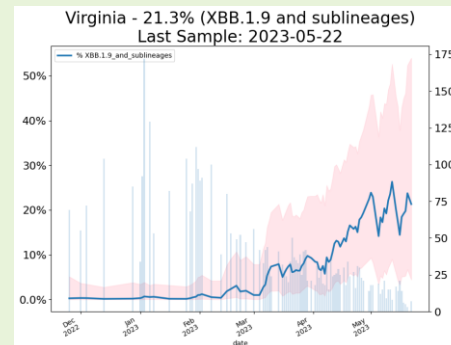
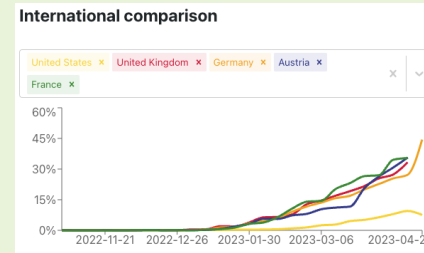
Enabled by data from **GISAID**

9-Jun-23

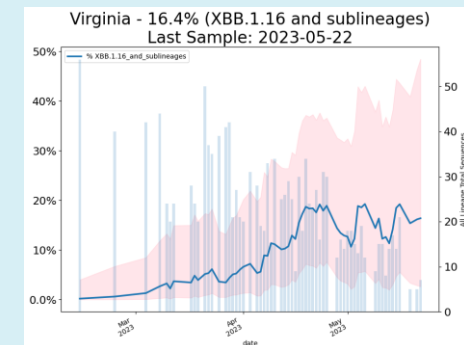
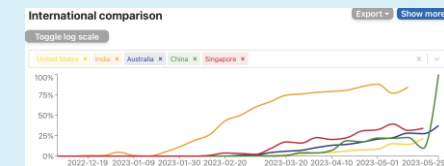
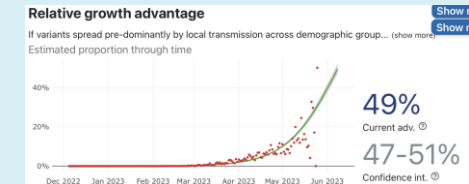
XBB.2.3*



XBB.1.9*



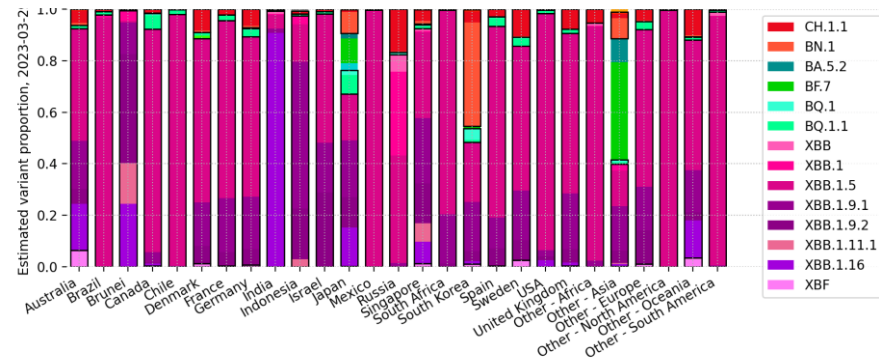
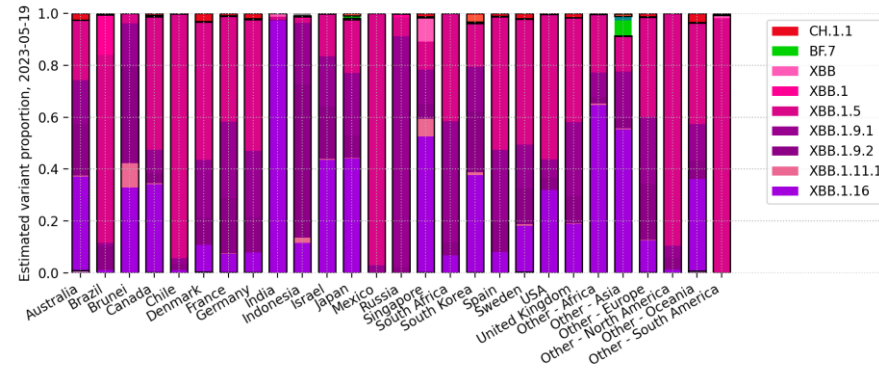
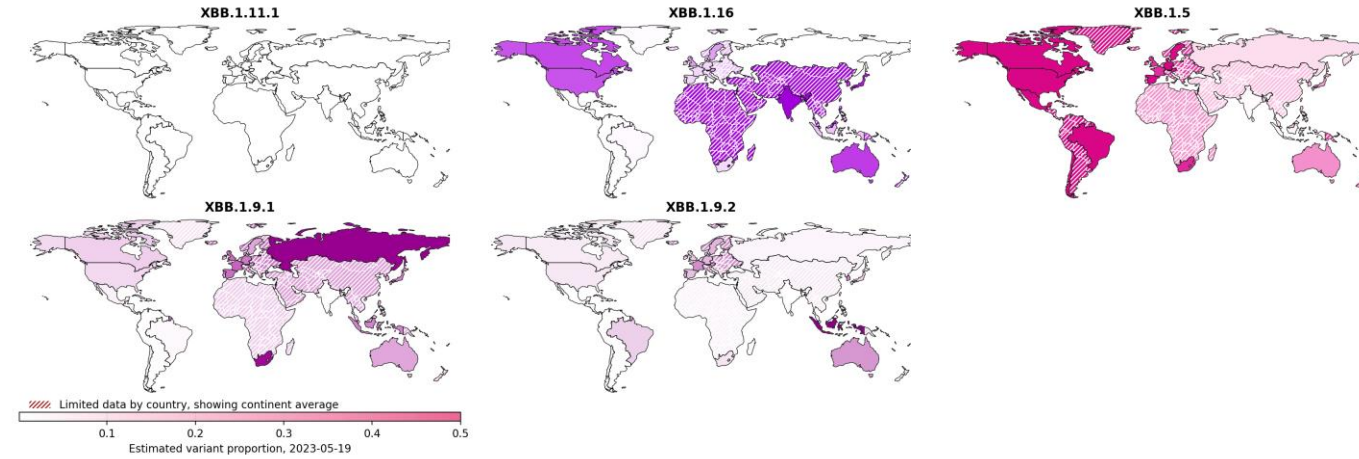
XBB.1.16*



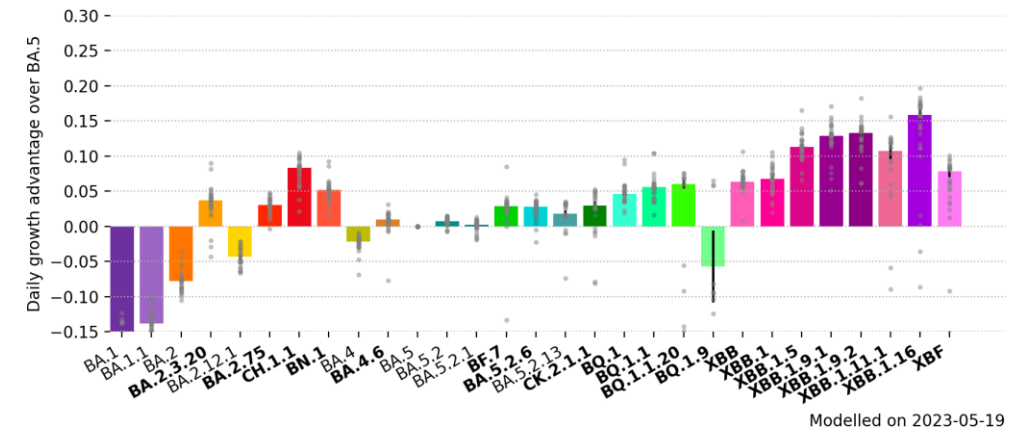
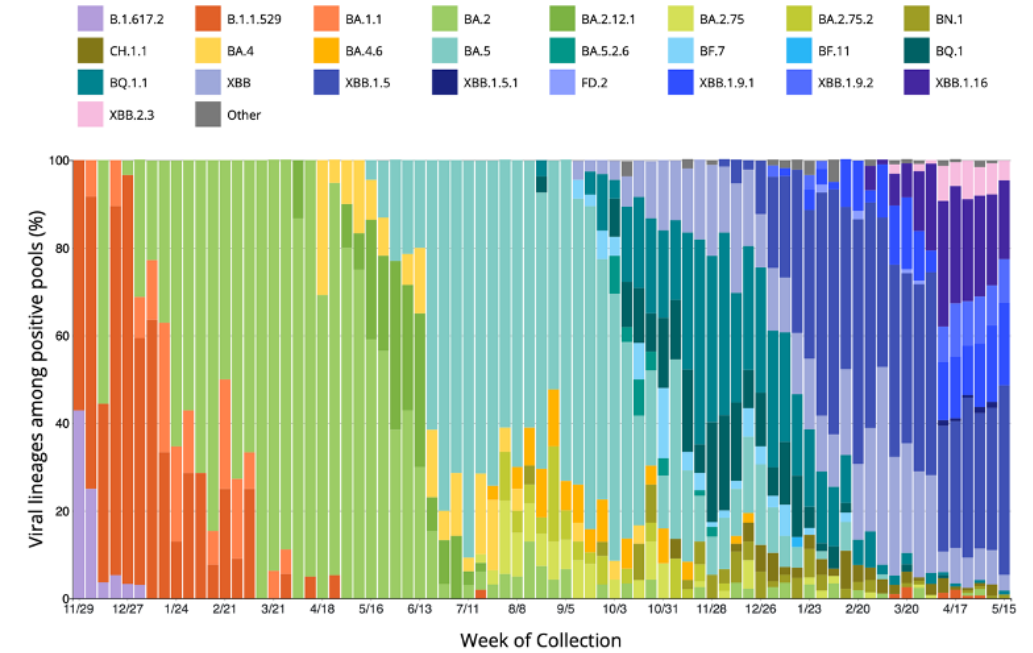
UNIVERSITY of VIRGINIA

BIOCOMPLEXITY INSTITUTE

Global SARS-CoV2 Variant Status



Variants Detected, by Collection Week



Modelled on 2023-05-19

<https://covid.cdc.gov/covid-data-tracker/#traveler-genomic-surveillance>

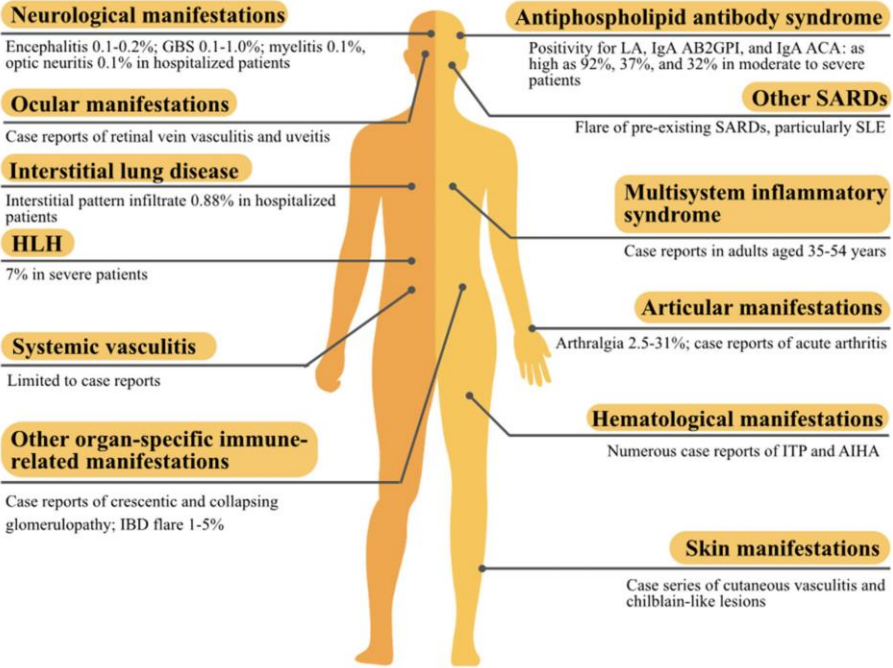
<https://github.com/gerstung-lab/SARS-CoV-2-International> (03/29/23)

Pandemic Pubs (June 8th, 2023)

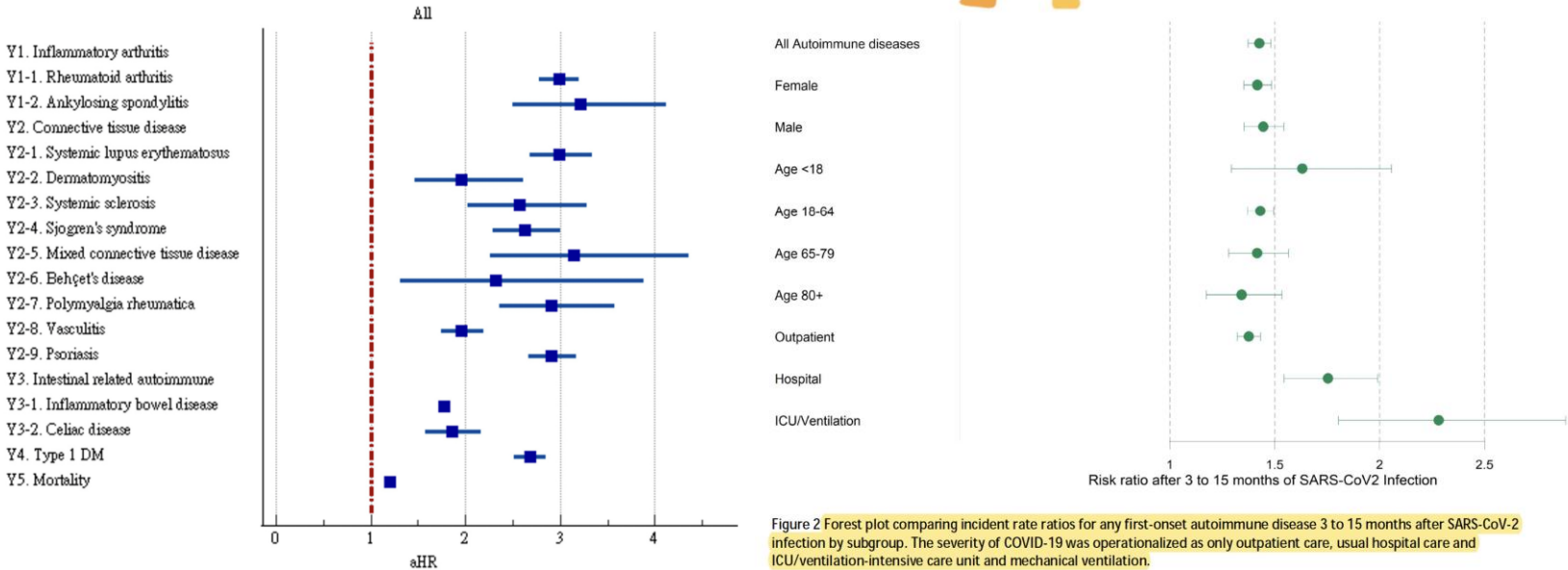
1. Several large cohort studies from different countries indicate and increased risk (20-30%) for new auto-immune disease following COVID-19 infection. One study shows increased risk based on severity of initial infection.

Study	N with Covid	N Controls No Covid	Increased Risk of New Autoimmune Disease	Citation
US	884,463	2,926,016	19-47%*	Chang R, eClinical Medicine, 9 January 2023
Germany	641,704	1,560,357	43%	Tesch F, MedRxiv, 26 January 2023
UK	458,147	1,818,929	22%	Syed U, MedRxiv 7 October 2022

*range dependent on specific autoimmune condition, adjusted for competing risks, before this adjustment 100-200% increased risk @erictopol



Severe COVID-19 cases have demonstrated a substantial inflammatory response with pro-inflammatory cytokines and chemokines that stimulate pulmonary inflammation. As the burden of COVID-19 cases increases worldwide, so does our understanding of the condition. Owing to worldwide vaccination efforts, mortality due to COVID-19 has been decreasing, but we continue to witness considerable morbidity and increased rates of post-COVID-19 conditions and in particular, new-onset autoimmune and inflammatory diseases in individuals who have had COVID-19. The range and incidence of these post-COVID-19 disorders have now been highlighted in two large retrospective cohort studies.



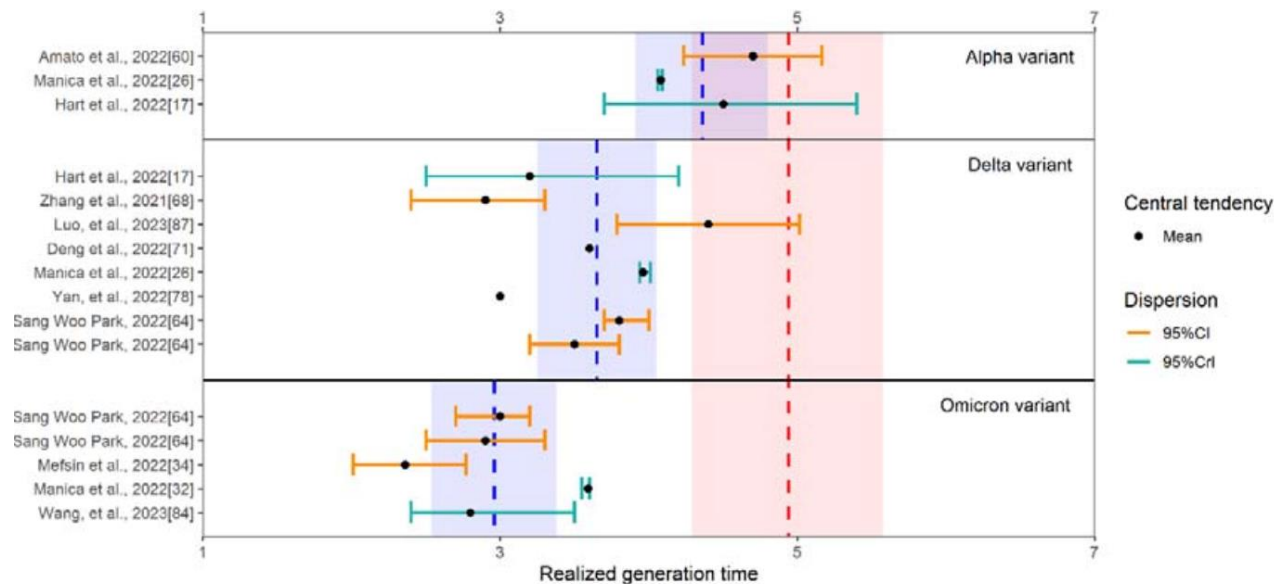
[Nature Reviews Rheumatology](https://www.nature.com/articles/s41584-023-00964-y)

<https://www.nature.com/articles/s41584-023-00964-y>

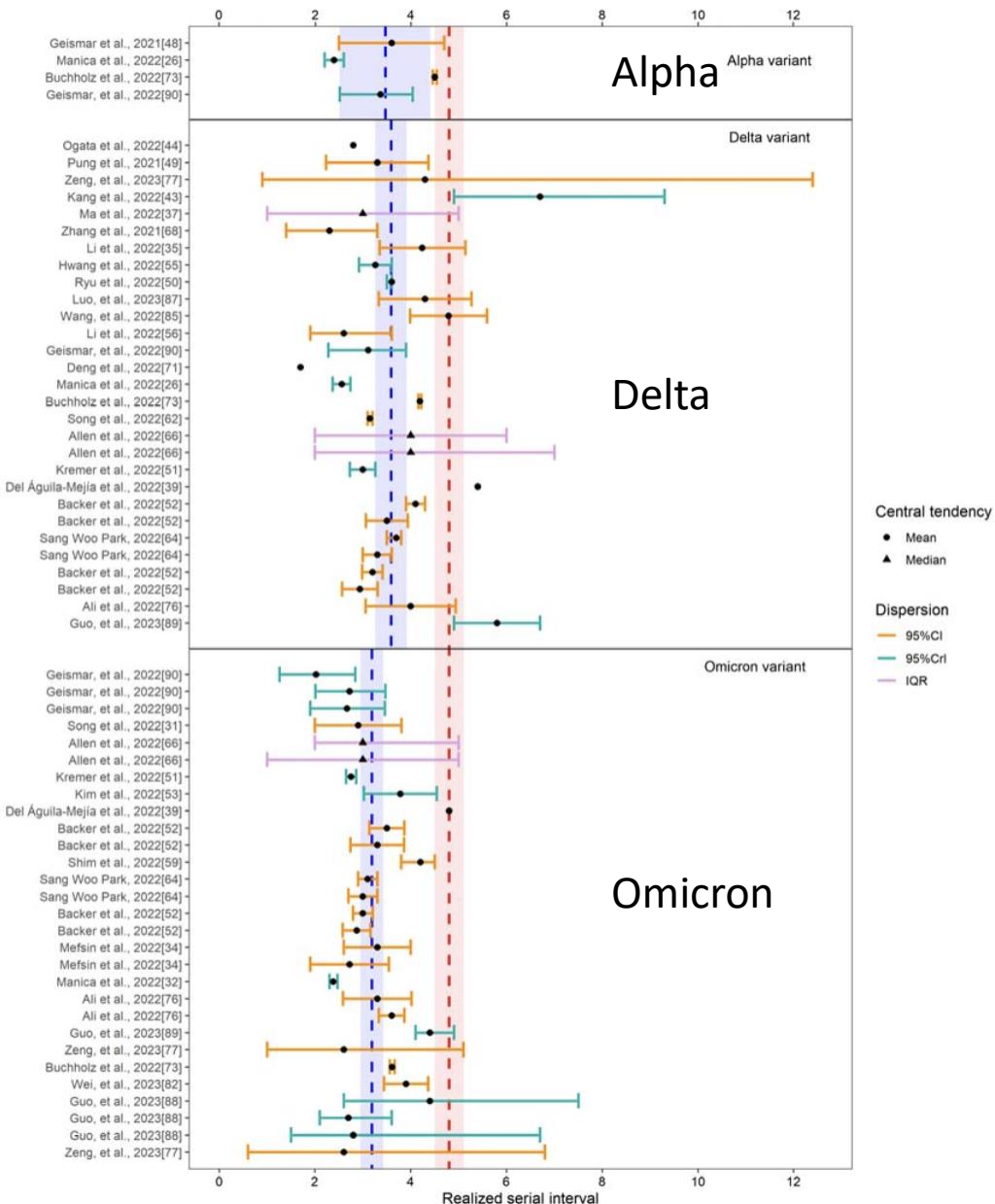
via [Eric Topol](#)

Pandemic Pubs (May 25th, 2023)

1. Meta-analysis derived pool of many household or contact tracing studies with well observed case series to further quantify the shortening of incubation and serial interval (time between infections) over time during the pandemic and across variants. Omicron’s serial interval is shorter than Delta which was similar to Alpha.

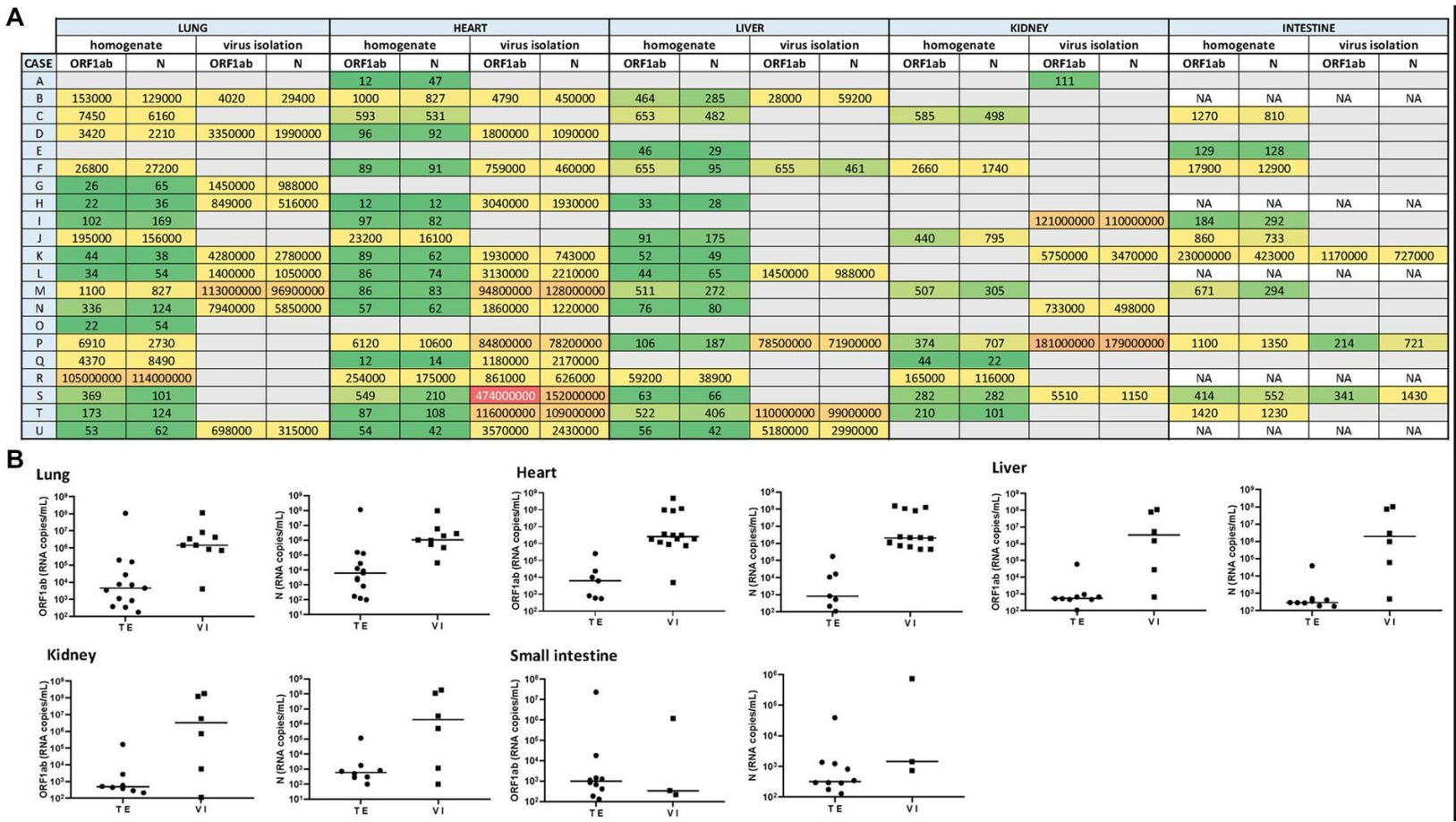


Omicron had the shortest pooled estimates for the incubation period (3.63 days, 95%CI: 3.25-4.02 days), serial interval (3.19 days, 95%CI: 2.95-3.43 days), and realized generation time (2.96 days, 95%CI: 2.54-3.38 days) whereas the ancestral lineage had the highest pooled estimates for each of them . We found considerable heterogeneities ($I^2 > 80\%$) when pooling the estimates across different virus lineages, indicating potential unmeasured confounding from population factors (e.g., social behavior, deployed interventions).



Pandemic Pubs (May 25th, 2023)

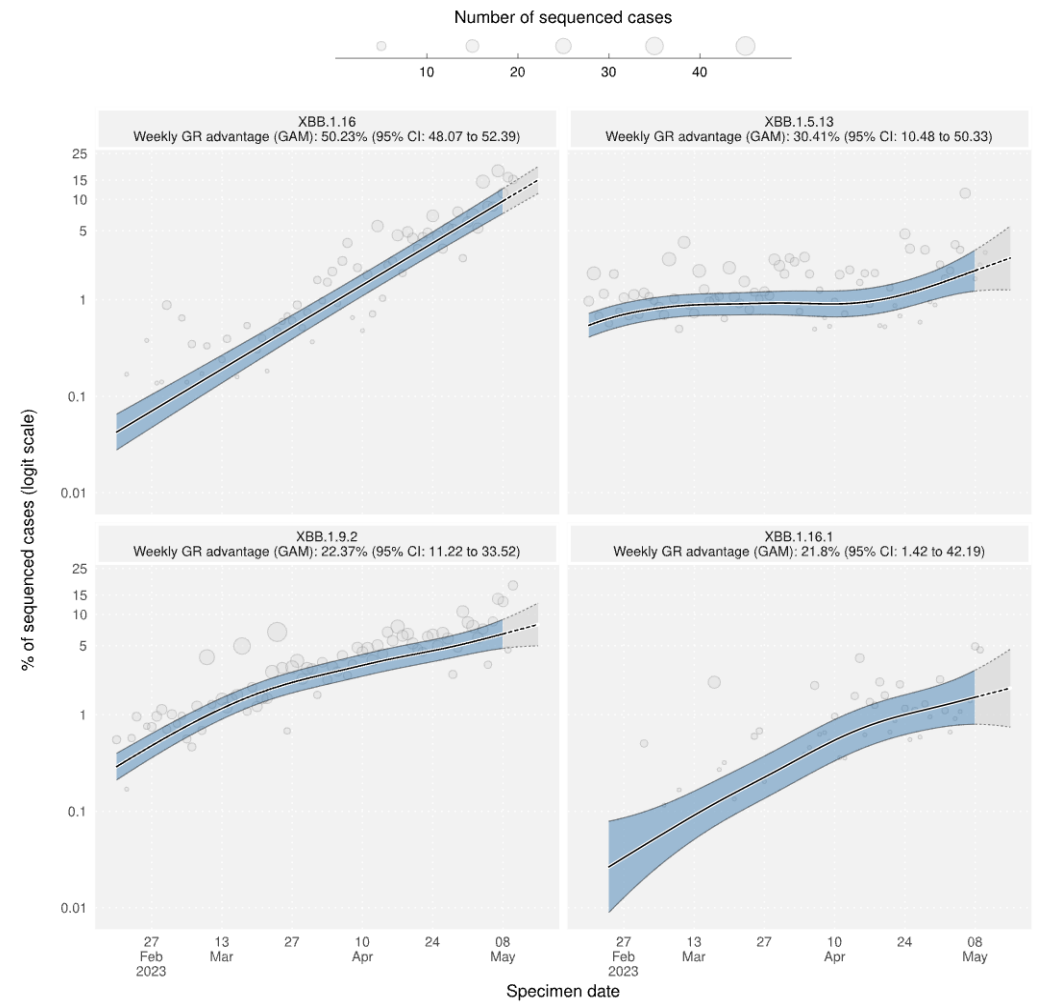
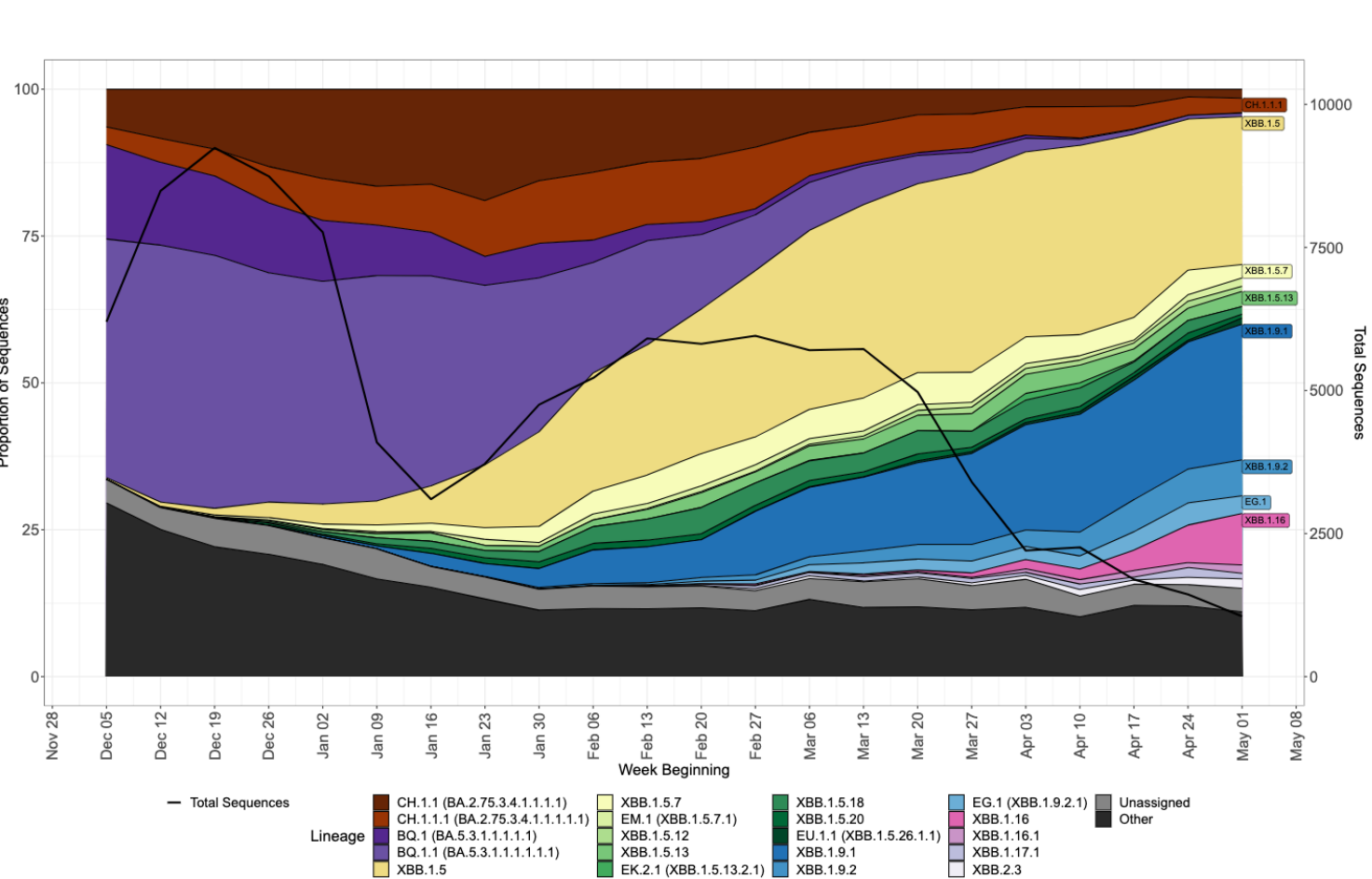
2. SARS-CoV-2 can spread to multiple tissues both after primary infection and reinfection. Further evidence of chronic infection leading to long Covid.



Researchers in Argentina autopsied 21 donors experience first infection or reinfection at time of death between January and August 2022. Their analysis shows persisting reservoirs of SARS-CoV-2 in multiple tissues including lungs, heart liver, kidneys and intestines with different characteristic loads after Omicron infection. Frequent causes of death included adult respiratory distress syndrome with bilateral lung compromise during COVID-19 as well as exacerbations of preexisting comorbidities and COVID-19. Genomes isolated from different tissues showed a remarkable amount of heterogeneity.

Pandemic Pubs (May 25th, 2023)

3. UKHSA prevalence and growth rate report shows a wide variety of variants and XBB.1.16 and XBB.1.19 having continued growth advantage



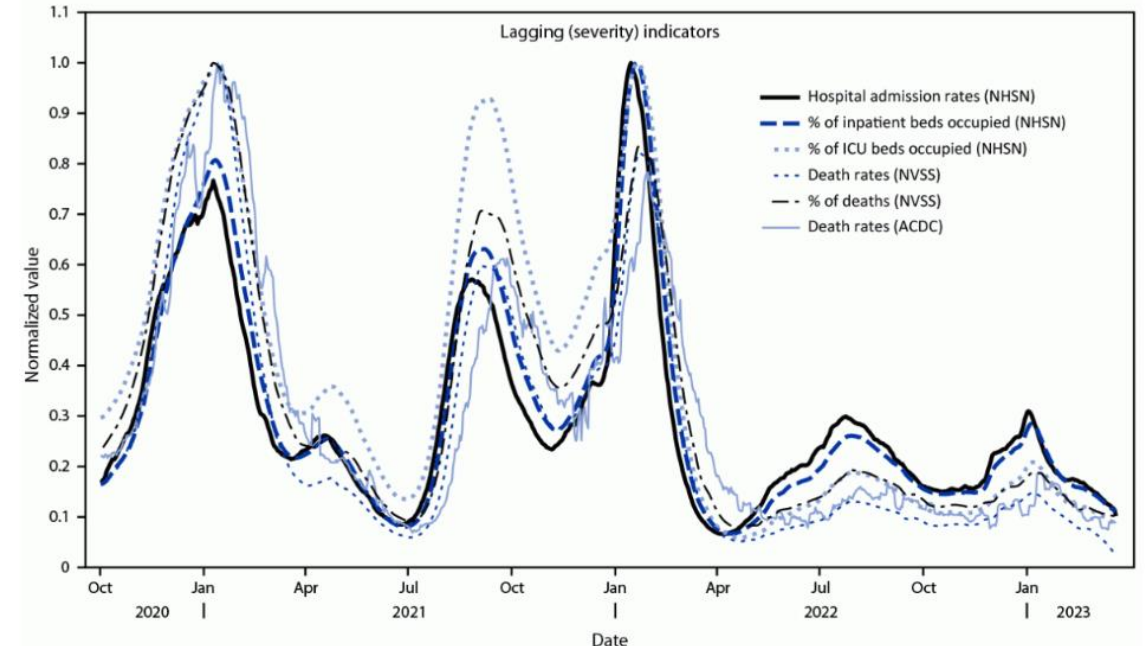
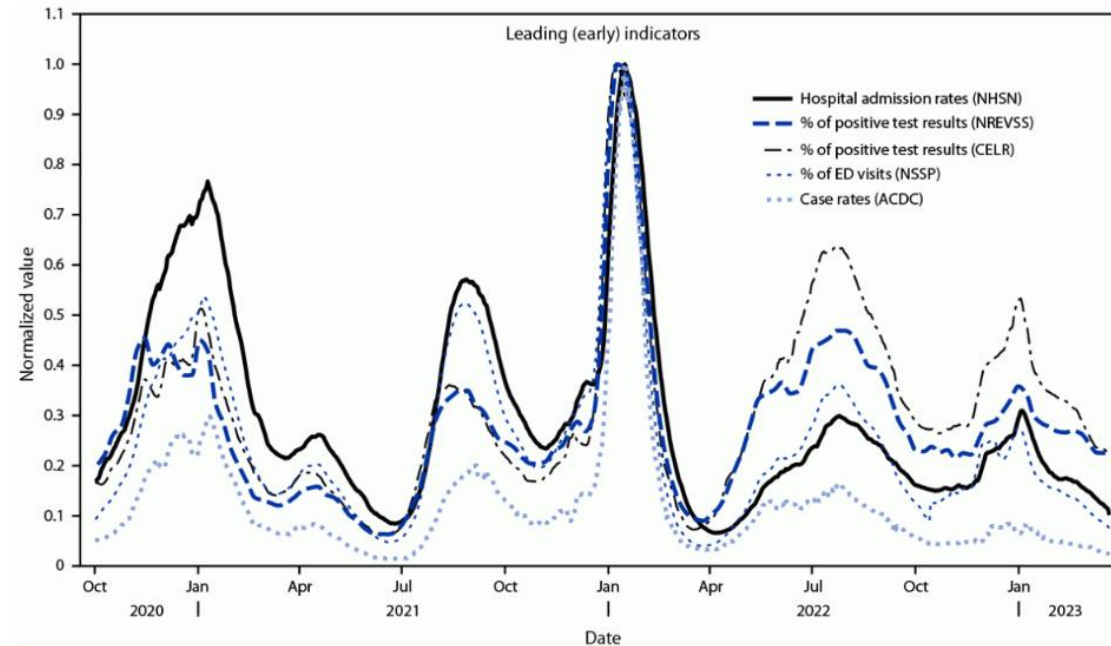
In the UK variant surveillance is now limited to individuals tested with PCR in hospitals with acute respiratory symptoms (plus a few research studies)

<https://www.gov.uk/government/publications/sars-cov-2-genome-sequence-prevalence-and-growth-rate/sars-cov-2-genome-sequence-prevalence-and-growth-rate-update-24-may-2023>

Pandemic Pubs (May 11th, 2023)

1. Positive test results, emergency department visits, and COVID-19 deaths are suitable and timely indicators of trends in COVID-19 activity and severity.

FIGURE. Trends in normalized values* of leading (A) and lagging (B)[†] COVID-19 surveillance indicators — United States, October 1, 2020–March 22, 2023

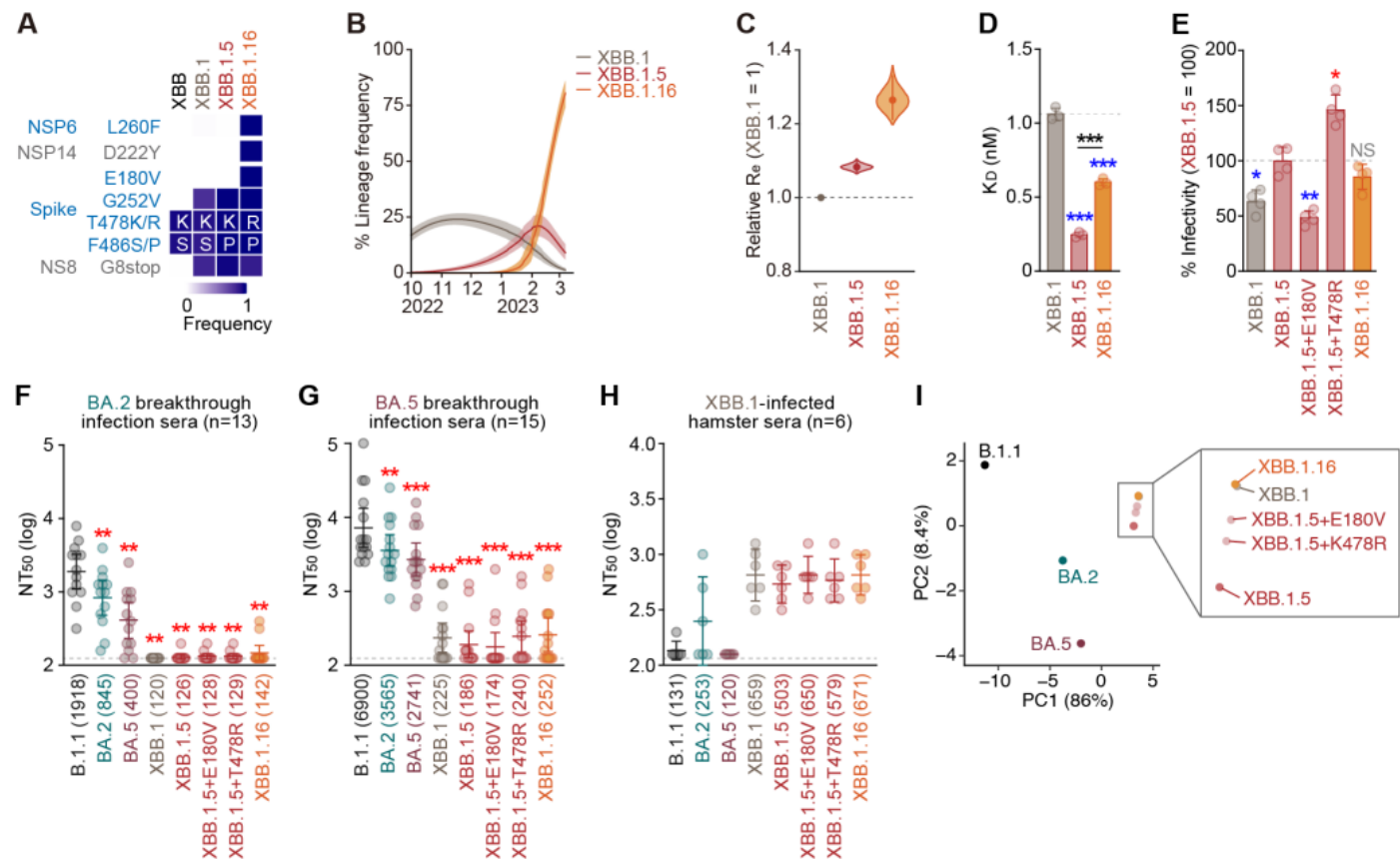


When the U.S. COVID-19 public health emergency declaration expires on May 11, 2023, national reporting of certain categories of COVID-19 public health surveillance data will be transitioned to other data sources or will be discontinued. Weekly COVID-19 Community Levels (CCLs) will be replaced with levels of COVID-19 hospital admission rates (low, medium, or high) which demonstrated >99% concordance by county during February 2022–March 2023. Authors suggest COVID-19–associated hospital admission levels are a suitable primary metric for monitoring COVID-19 trends

https://www.cdc.gov/mmwr/volumes/72/wr/mm7219e2.htm?s_cid=mm7219e2_x#contribAff

Pandemic Pubs (April 19th, 2023)

1. XBB.1.16 shows a similar resistance profile to XBB.1 and XBB.1, in that it is resistant to a variety of anti-SARS-CoV-2 antibodies from breakthrough infections. Scientists suggest this parity indicates it's growth advantage may come from some other transmission property such as a change in antigenicity or in viral growth efficiency.



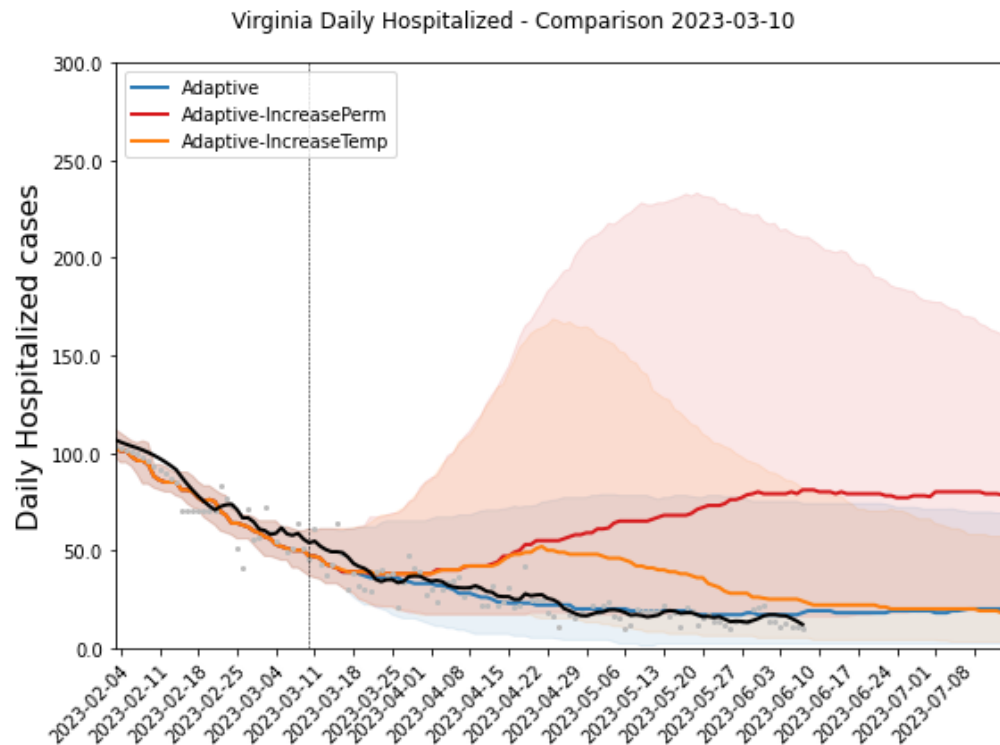
Scientists in Japan characterized the antibody neutralization of XBB.1.16. Panels F, G, H indicate as similar neutralization profile to other XBB variants relative to breakthrough infections. Panels D and E show the ACE2 binding affinity and infectivity respectively. A change in antigenicity relative to XBB 1.5 is inferred from a PCA of neutralization assays F and G (neutralization cartography).

Model Results

Past projections – Hospitalizations

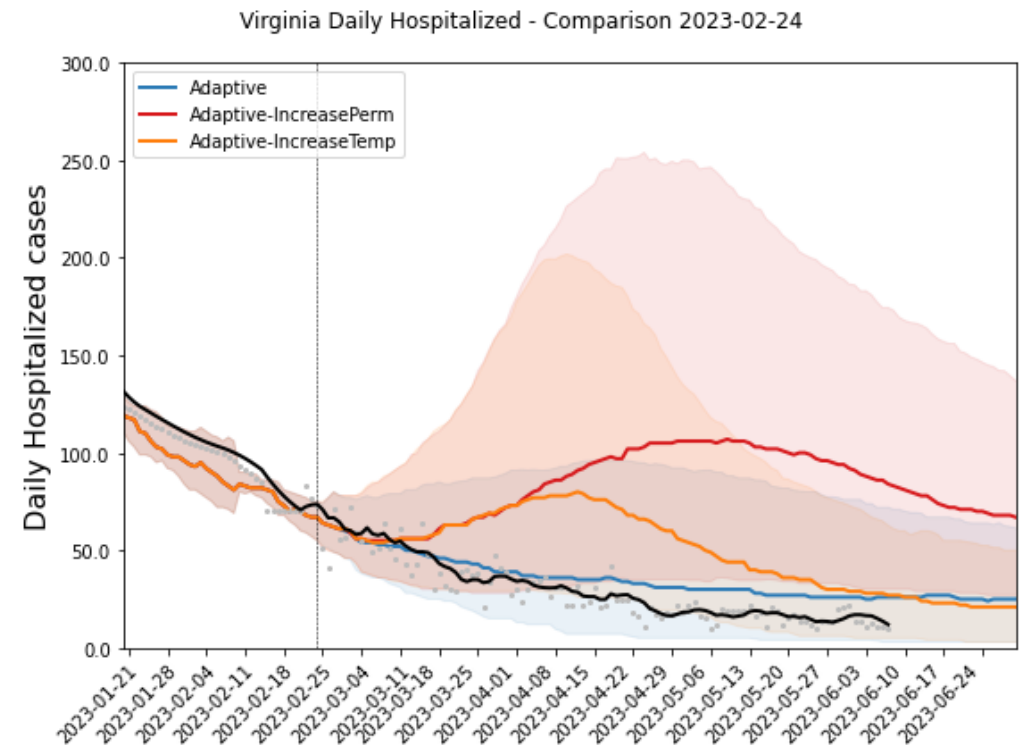
- Previous projections remain on target with recent observations
- Past 14 weeks have stayed steady and indicate possibility of slight upward trend in coming weeks

Previous round – 14 weeks ago



9-Jun-23

Previous round – 16 weeks ago



41

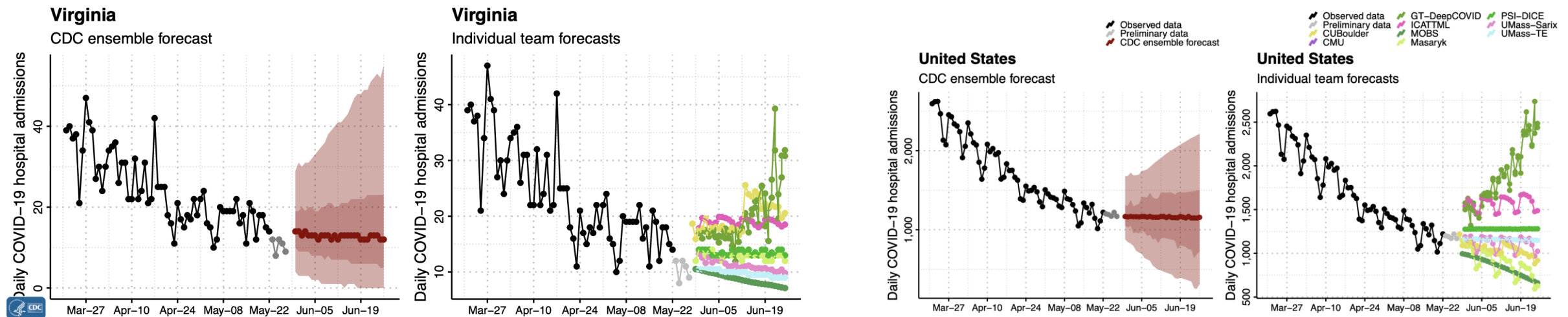
National Modeling Hub Updates

Current COVID-19 Hospitalization Forecast

Statistical models for submitting to CDC COVID Forecasting Hub

- Uses a variety of statistical and ML approaches to forecast weekly hospital admissions for the next 4 weeks for all states in the US

Hospital Admissions for COVID-19 and Forecast for next 4 weeks (CDC COVID Ensemble)



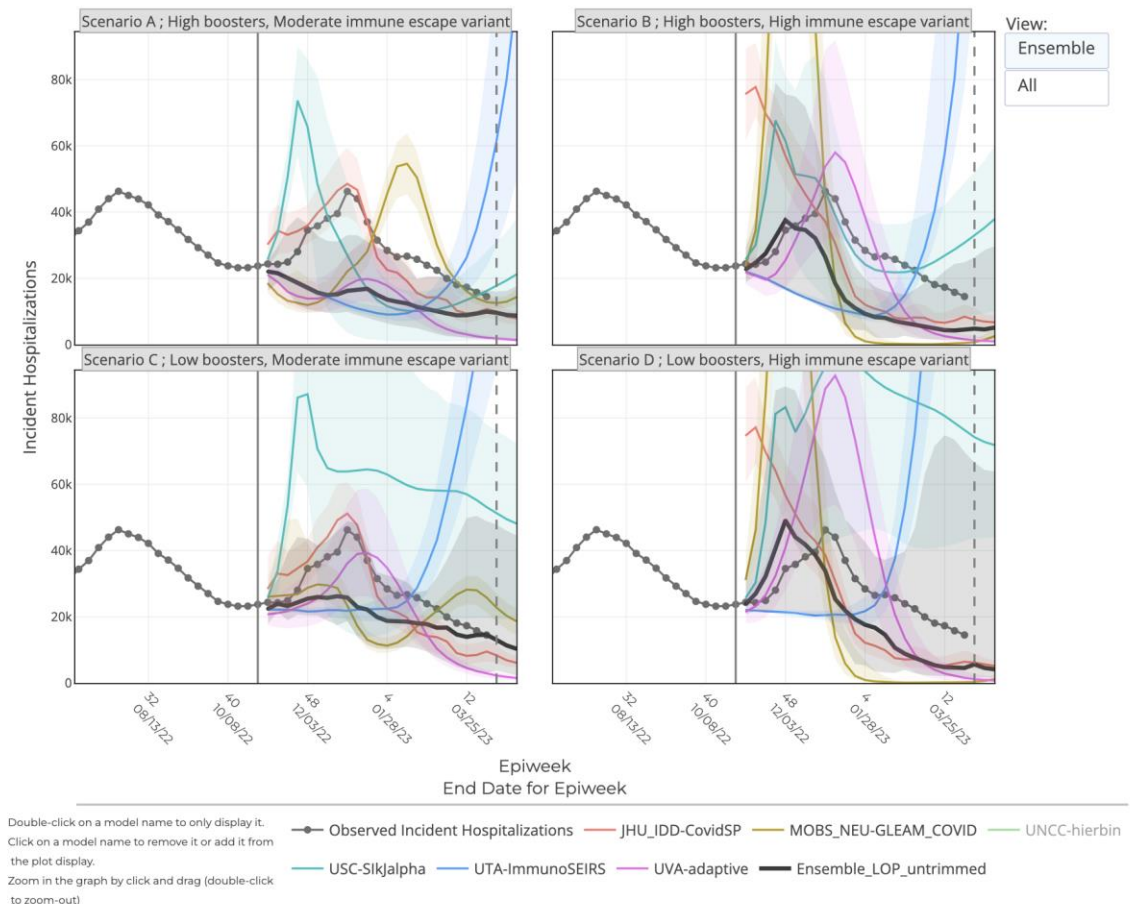
Scenario Modeling Hub – COVID-19 (Round 16)

Collaboration of multiple academic teams to provide national and state-by-state level projections for 4 aligned scenarios

- Round 16 results published
- Moderate escape scenarios tracking best
- Round 17 is underway, prelim results in coming weeks

<https://covid19scenariomodelinghub.org/viz.html>

Projected Incident Hospitalizations by Epidemiological Week and by Scenario for Round 16 - US
(- Projection Epiweek; -- Current Week)



	"Level 5" Variants	"Level 6/7" Variants
Accelerating uptake levels of reformulated boosters	<p>Scenario A</p> <p>"Level 5" Variants</p> <ul style="list-style-type: none"> - Variants have a 25% immune escape from BA.5.2 - Seeding based on combined observed prevalence of Level 5 variants at the start of the projection period - No change in severity given symptomatic infection <p>Accelerating uptake levels of reformulated boosters, with coverage plateauing at 90% of flu vaccination levels by February 1st, 2023</p> <ul style="list-style-type: none"> - Teams are free to use available data and information from current and previous rollouts as they see fit to define rates - Teams should assume increasing uptake through October and November as necessary to reach the projected February 1st, 2022 plateau 	<p>Scenario B</p> <p>"Level 6/7" Variants</p> <ul style="list-style-type: none"> - Variants have a 50% immune escape from BA.5.2 - Seeding based on combined observed prevalence of Level 6 and 7 variants at the start of the projection period - No change in severity given symptomatic infection <p>Accelerating uptake levels of reformulated boosters, with coverage plateauing at 90% of flu vaccination levels by February 1st, 2023</p> <ul style="list-style-type: none"> - Teams are free to use available data and information from current and previous rollouts as they see fit to define rates - Teams should assume increasing uptake through October and November as necessary to reach the projected February 1st, 2022 plateau
Current uptake levels of reformulated boosters	<p>Scenario C</p> <p>"Level 5" Variants</p> <ul style="list-style-type: none"> - Variants have a 25% immune escape from BA.5.2 - Seeding based on combined observed prevalence of Level 5 variants at the start of the projection period - No change in severity given symptomatic infection <p>Current uptake levels of reformulated boosters, with coverage plateauing at booster 1 levels by the end of the simulation</p> <ul style="list-style-type: none"> - Teams are free to use available data and information from current and previous rollouts as they see fit to define rates - Based on current rates, plateau date is flexible as long as it occurs before the end of the simulation (Teams can adjust rates up if needed to achieve adequate coverage by target date) 	<p>Scenario D</p> <p>"Level 6/7" Variants</p> <ul style="list-style-type: none"> - Variants have a 50% immune escape from BA.5.2 - Seeding based on combined observed prevalence of Level 6 and 7 variants at the start of the projection period - No change in severity given symptomatic infection <p>Current uptake levels of reformulated boosters, with coverage plateauing at booster 1 levels by the end of the simulation</p> <ul style="list-style-type: none"> - Teams are free to use available data and information from current and previous rollouts as they see fit to define rates - Based on current rates, plateau date is flexible as long as it occurs before the end of the simulation (Teams can adjust rates up if needed to achieve adequate coverage by target date)

Scenario Modeling Hub – COVID-19 (Round 17)

Collaboration of multiple academic teams to provide national and state-by-state level projections for 6 aligned scenarios

<https://covid19scenariomodelinghub.org/viz.html>

- Preliminary Results
- Round Designed to explore different seasonal vaccination levels and the impact of Immune Escape

Scenario Dimensions:

Immune Escape (IE):

Slower IE (20%/yr) vs.
Faster IE (50%/yr)

Vaccination levels:

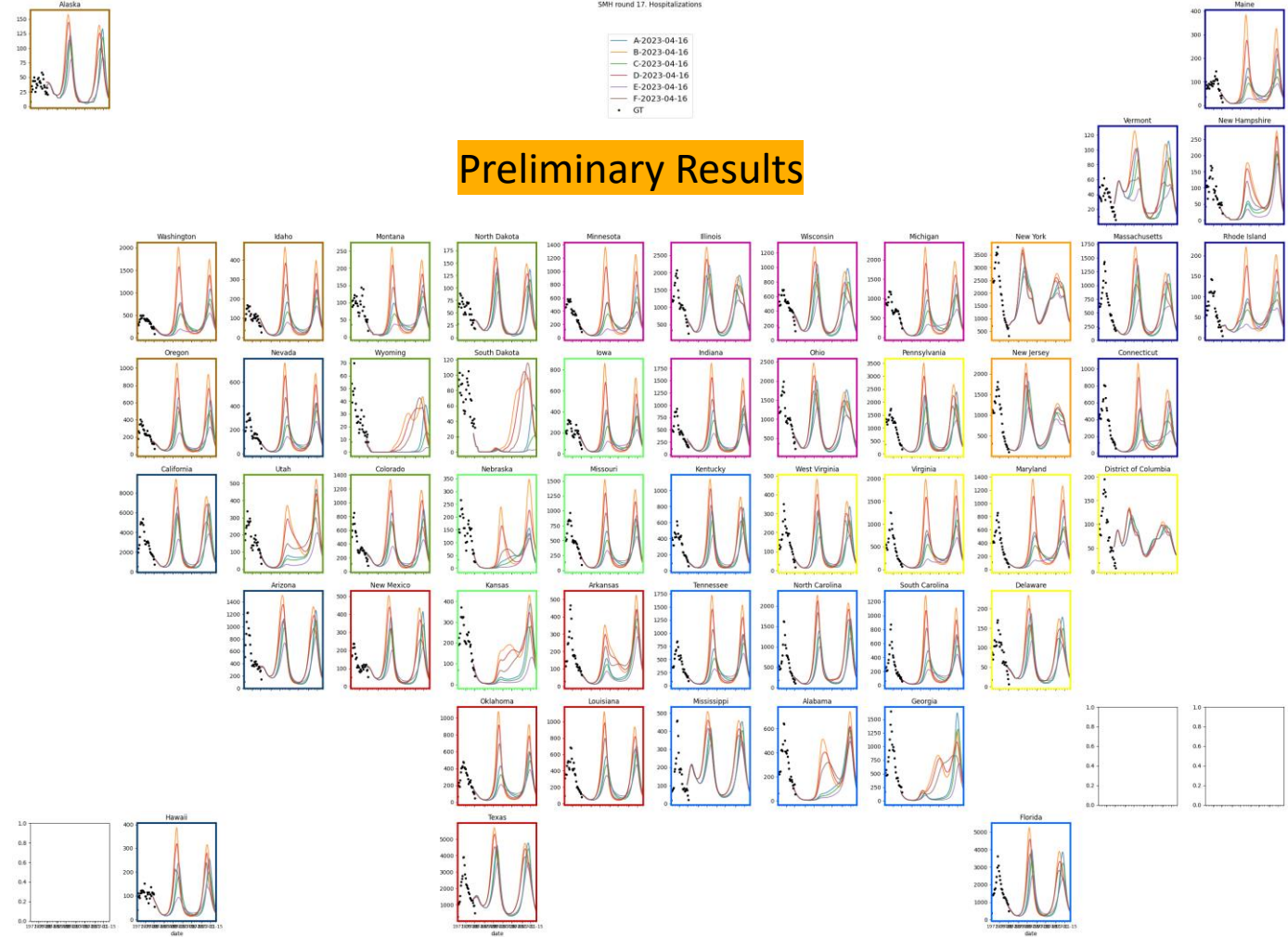
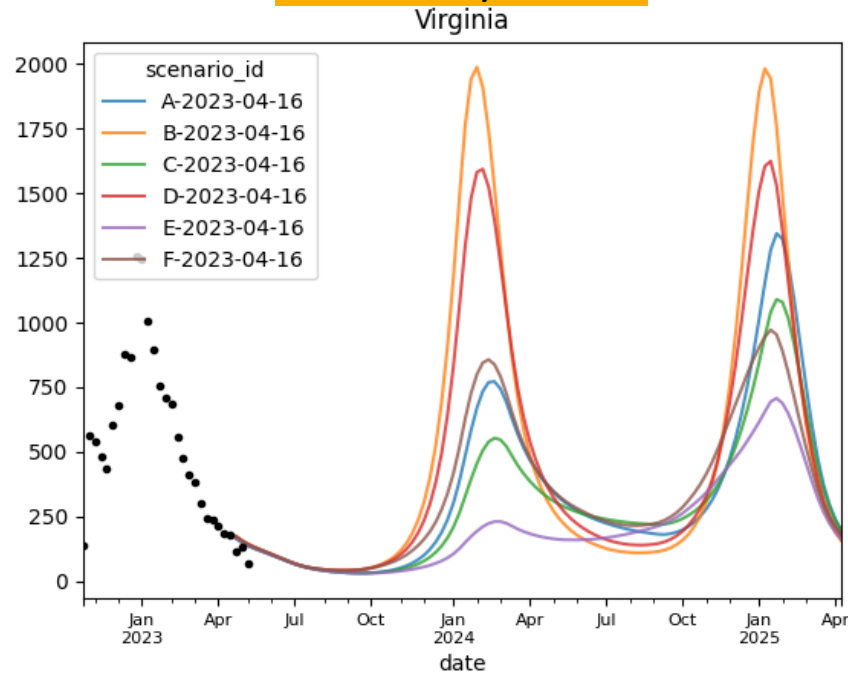
None vs.
Vulnerable and 65 + vs.
Broader population of eligible

	Low immune escape <ul style="list-style-type: none">• Immune escape occurs at a constant rate of 20% per year	High immune escape <ul style="list-style-type: none">• Immune escape occurs at a constant rate of 50% per year
No vaccine recommendation <ul style="list-style-type: none">• Uptake negligible or continues at very slow levels based on existing 2022 booster trends	Scenario A	Scenario B
Reformulated annual vaccination recommended for 65+ and immunocompromised <ul style="list-style-type: none">• Reformulated vaccine has 65% VE against variants circulating on June 15• Vaccine becomes available September 1• Uptake in 65+ same as first booster dose recommended in September 2021• Uptake in individuals under 65 negligible or continues to trickle based on 2022 booster trends	Scenario C	Scenario D
Reformulated annual vaccination recommended for all currently eligible groups <ul style="list-style-type: none">• Reformulated vaccine has 65% VE against variants circulating on June 15• Vaccine becomes available September 1• 65+ uptake same as first booster dose recommended in September 2021• Coverage in individuals under 65+ saturates at levels of the 2021 booster (approximately 34% nationally)	Scenario E	Scenario F

UVA model – Preliminary Results (Round 17)

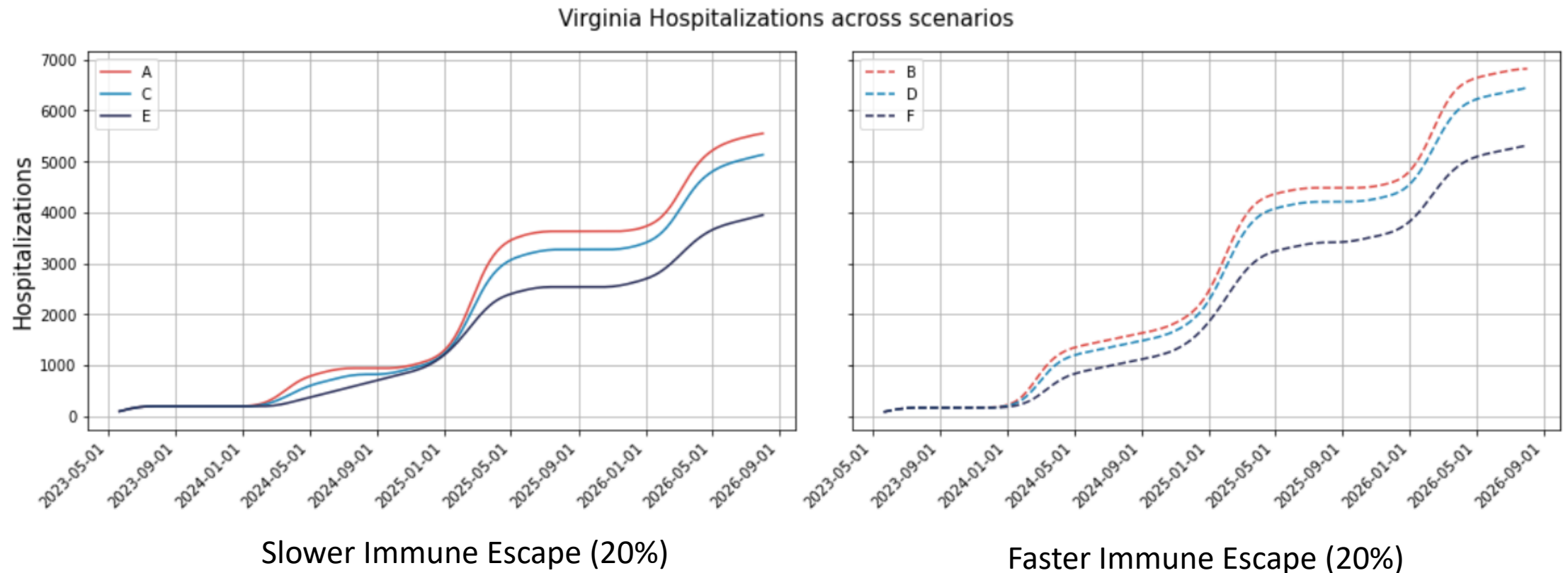
- Vaccination drives down hospitalizations
- Broad population vax levels akin to bivalent booster significantly reduce hospitalizations

Preliminary Results



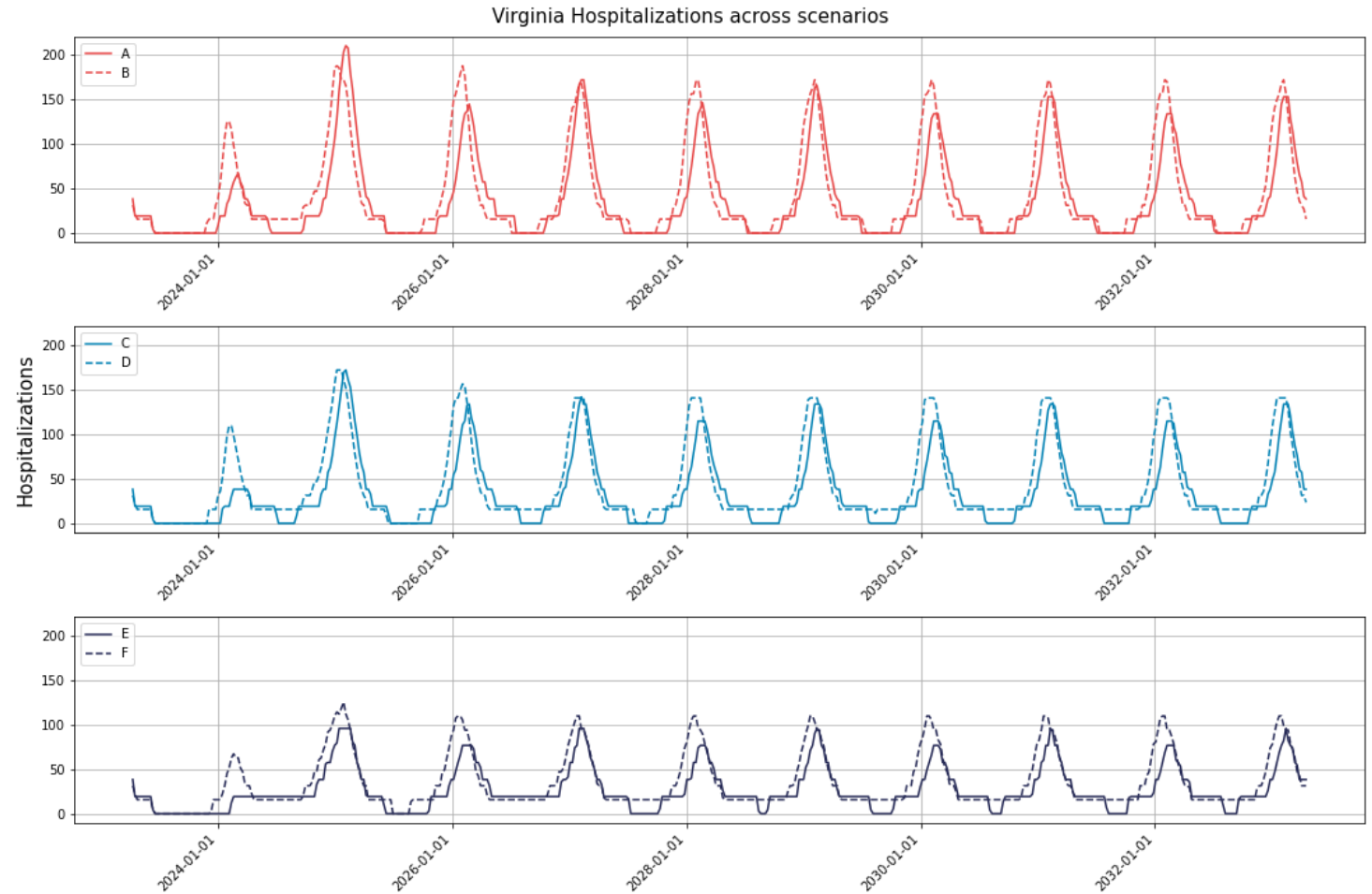
UVA model – Preliminary Results (Round 17)

- Cumulative hospitalizations over 2 years shows spread across vaccination levels
- Broad annual vaccination campaign reduces hospitalizations by 27% over 2 years



UVA model – Preliminary Results (Round 17)

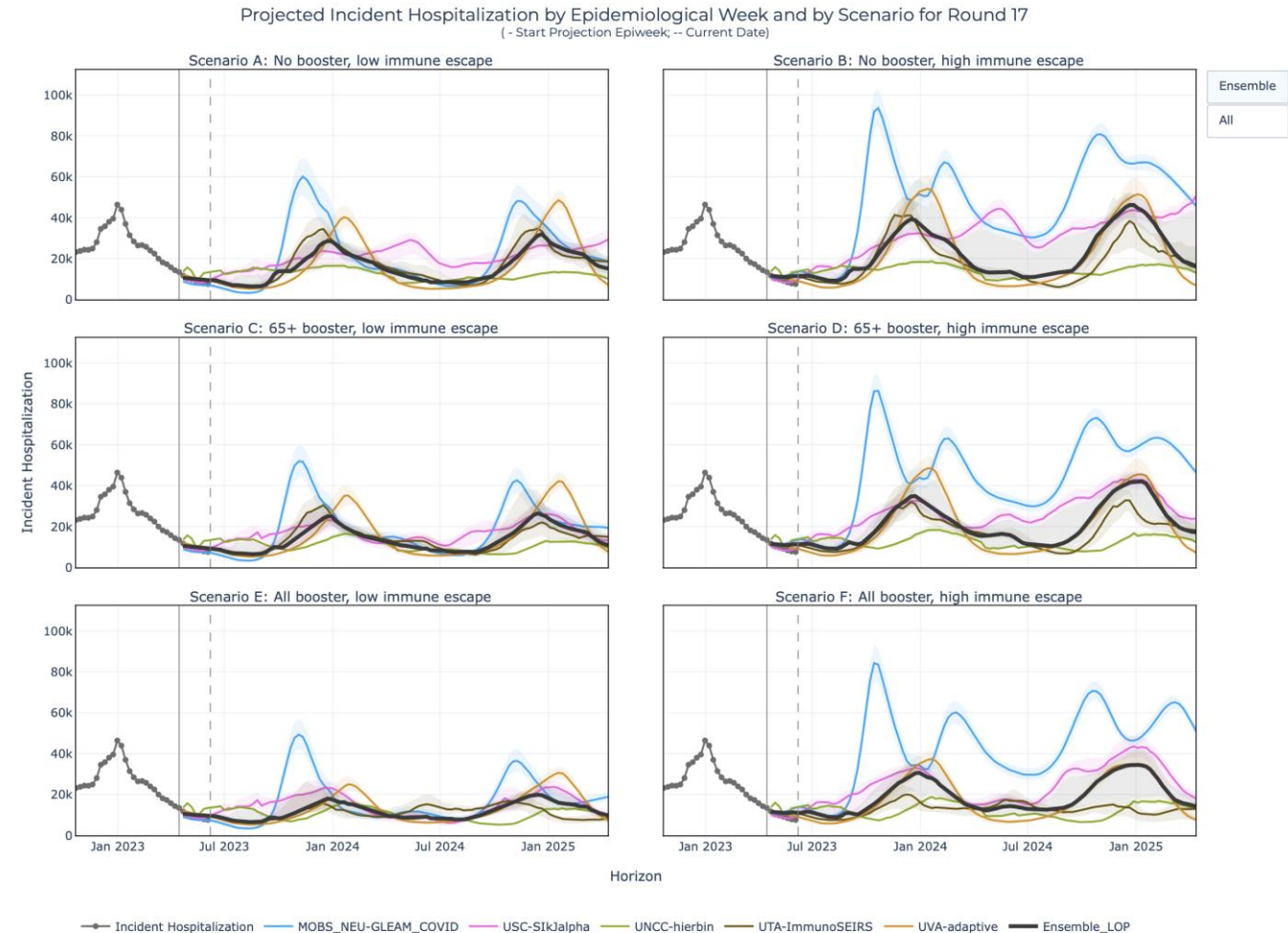
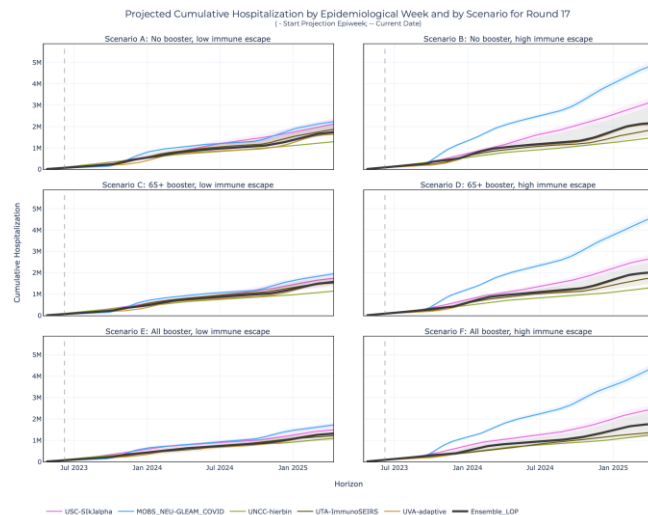
- Peak timing and size can oscillate over the longer term
- These scenarios are very unlikely to remain stable over longer term, nonetheless, some of these patterns may remain
- Scenarios with faster immune escape (dashed) converge more quickly than the slower immune escape



Preliminary Results

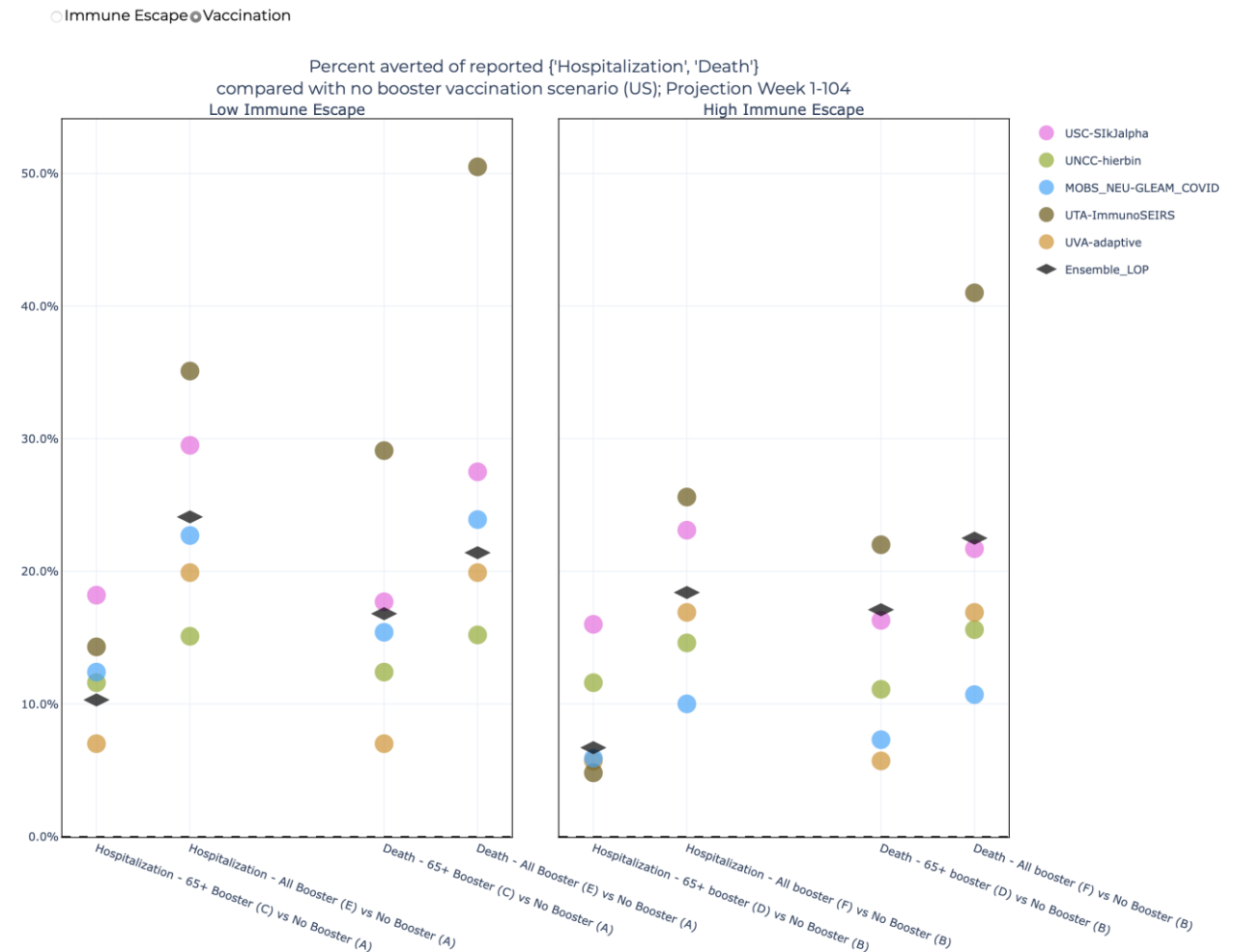
SMH summary – Preliminary Results (Round 17)

- Most models show similar seasonal patterns though many don't return to very low levels in the “inter-season” period
- Peak sizes vary considerably between models, however, cumulative hospitalizations cluster tighter



SMH summary – Preliminary Results (Round 17)

- Models estimate potential reduction in hospitalizations ranging from 35% - 15% for a whole population campaign and 8% - 18% for a 65+ only campaign
- Reductions in deaths are higher with ensemble estimates of 22% reduction for whole population and 18% reduction for 65+
- Reductions are smaller for the high immune escape scenarios

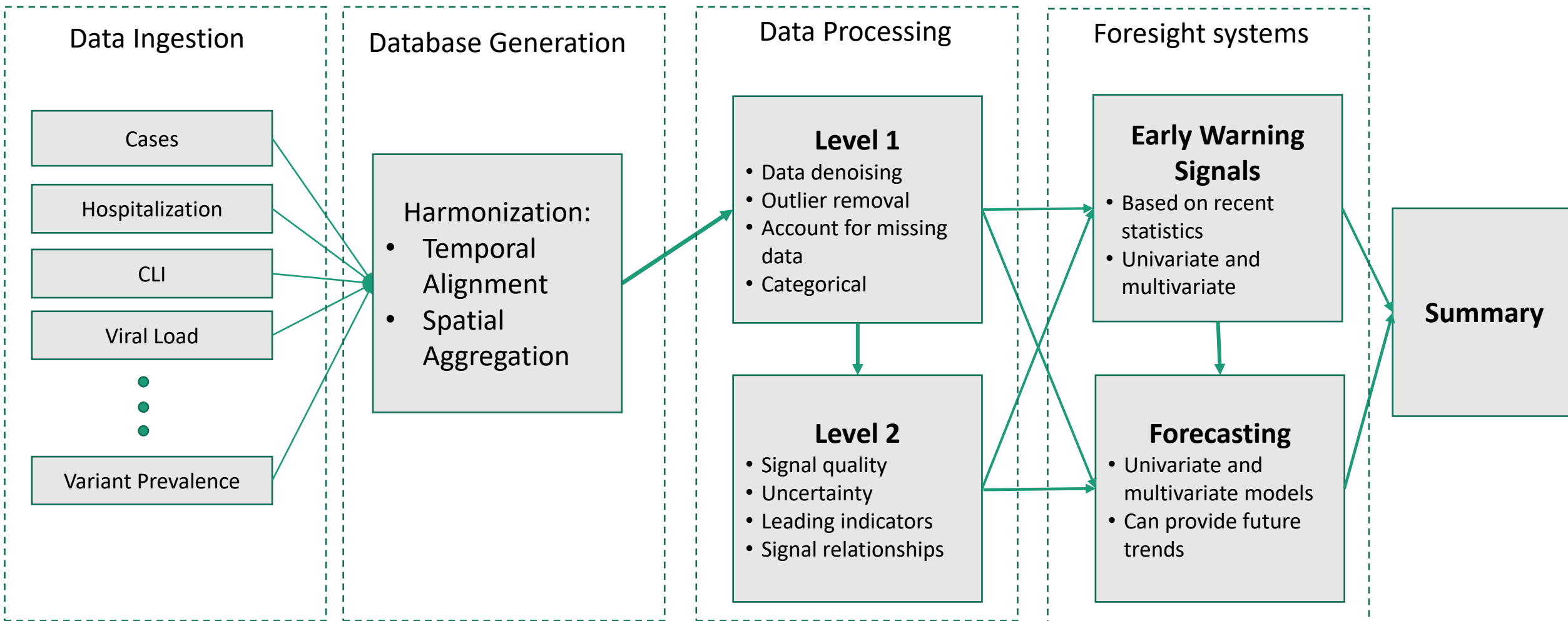


Fusing Multiple Biosurveillance Metrics at Different Resolutions Research Update

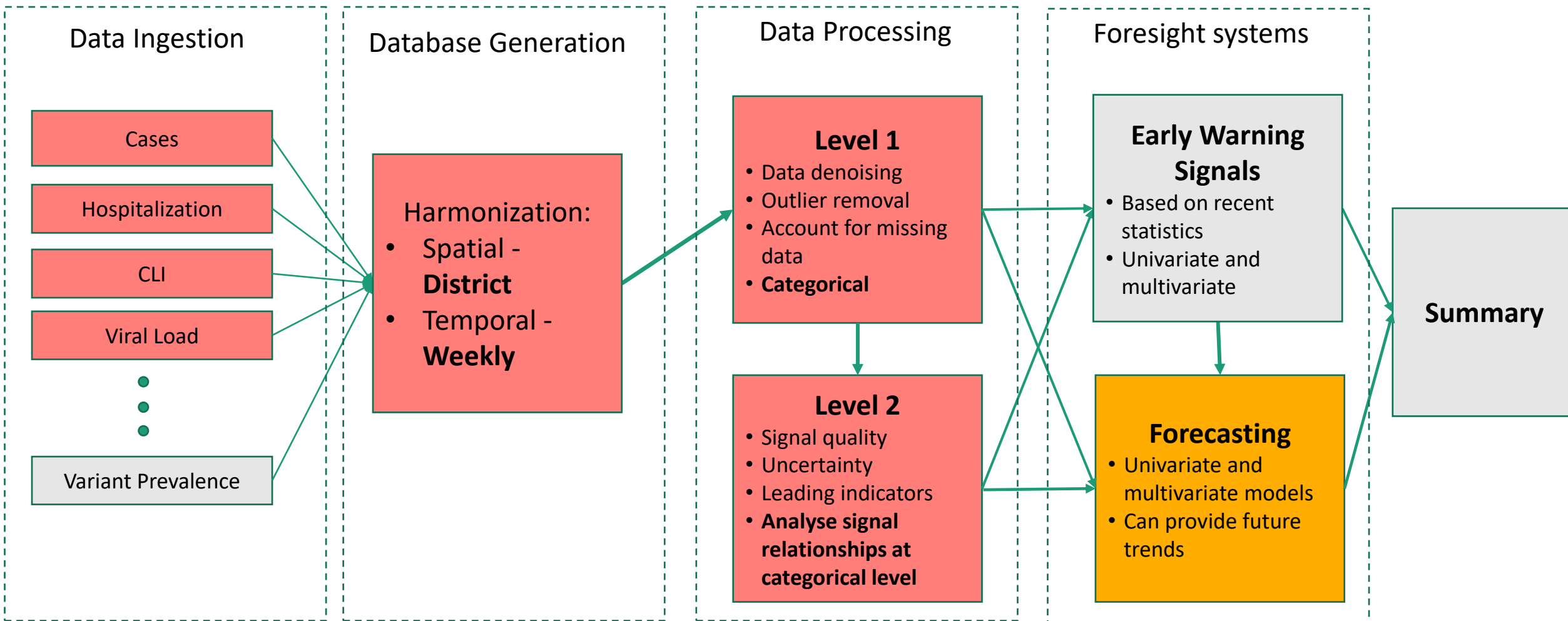
Summary

- **Categorical indicator methods & analytics**
 - Analyzing signals at the categorical level.
 - Categorization based on quantiles
 - Understand different signals at District resolution
 - Time series analysis, regression and [forecasting](#)
- **Statistical tests to assess the significance of associations between variables**
 - Variable selection for the modeling purposes

Biosurveillance System Components

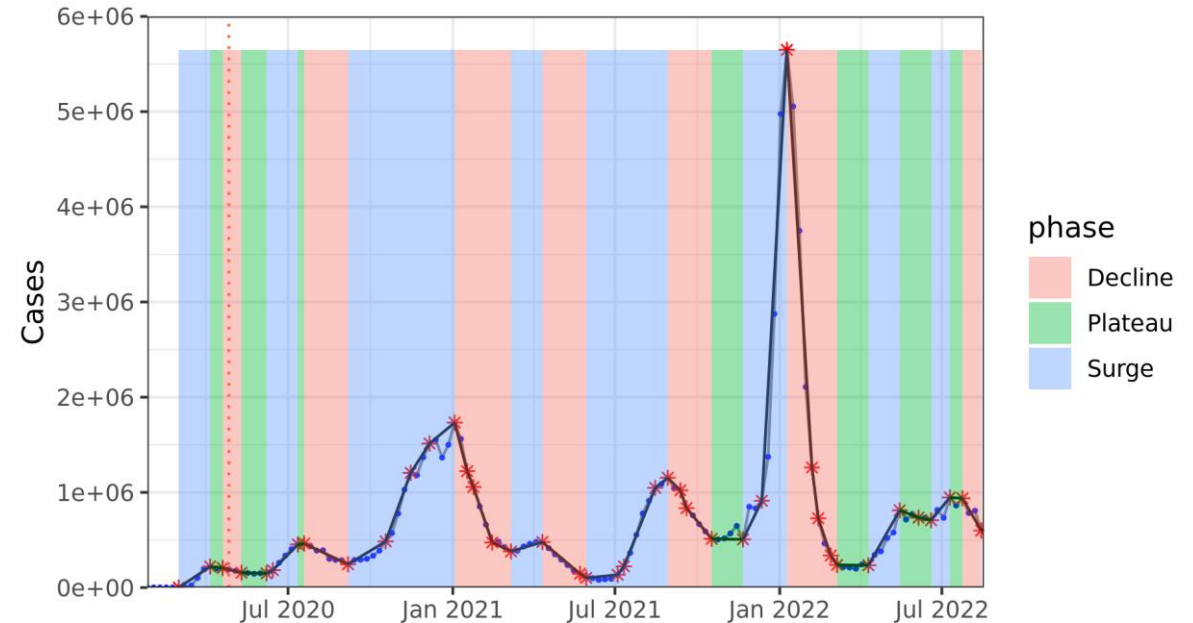


Biosurveillance System Components



Categorical Indicators

1. Level-based categories: determining bin boundaries based on
 - a) K quantiles using the entire time series
 - b) Equal bins : by dividing the data into K equal bins
2. **Trend based categories:** based on rate of change (ROC)
 - a) from recent change point – uses only data from change point [1]
 - b) In a **fixed length window**
 - **Surge** ($\text{ROC} > +10\%$)
 - **Decline** ($\text{ROC} < -10\%$)
 - **Plateau** (otherwise)



[1] Phase-Informed Bayesian Ensemble Models
Improve Performance of Covid-19 Forecasts. IAAI 2023.

Test of association between Cases and Viral Load

- To test if there is any significant association between two categorical variables

Observed frequency

Quantile Category Cases	Quantile Category Viral Load			Total
	Low	Med	High	
Low	446	192	68	706
Med	189	281	222	692
High	71	219	398	688
Total	706	692	688	2086

Expected frequency

Quantile Category Cases	Quantile Category Viral Load			Total
	Low	Med	High	
Low	239	234	233	706
Med	234	230	228	692
High	233	228	227	688
Total	706	692	688	2086

- Uniform marginal and joint densities** for quantile-based categories
- Viral load and Cases are not independent
 - $\chi^2 = 566.028$, $df = 4$, $p\text{-value} = 0.00$

Test of association with CLI and hospitalizations

H_0 : Cases are **independent** of CLI

Quantile Category Cases	Quantile Category CLI			Total
	Low	Med	High	
Low	460 65.2%	160 22.7%	86 12.2%	706 100%
Med	181 26.2%	318 46%	193 27.9%	692 100%
High	65 9.4%	214 31.1%	409 59.4%	688 100%
Total	706	692	688	2086

- $\chi^2 = 640.228$, $df = 4$, p-value= 0.00
- Reject H_0 : Cases are **not** independent of CLI

H_0 : Cases are **independent** of Hospitalizations

Quantile Category Cases	Quantile Category hospitalizations			Total
	Low	Med	High	
Low	511 72.4%	166 23.5%	29 4.1%	706 100%
Med	162 23.4%	329 47.5%	201 29%	692 100%
High	33 4.8%	197 28.6%	458 66.6%	688 100%
Total	706	692	688	2086

- $\chi^2 = 987.028$, $df = 4$, p-value = 0.00
- Reject H_0 : Cases are **not** independent of Hospitalizations

Multinomial logistic regression model

$$\eta(qnt_cases) = \beta_0 + \beta_1 qnt_vl$$

Two logistic models for a categorical variable with 3 values:

i. $\log\left(\frac{P(qnt_cases=2)}{P(qnt_cases=1)}\right) = \beta_{2,0} + \beta_{2,1}I_{qnt_vl2} + \beta_{2,2}I_{qnt_vl3}$

ii. $\log\left(\frac{P(qnt_cases=3)}{P(qnt_cases=1)}\right) = \beta_{3,0} + \beta_{3,1}I_{qnt_vl2} + \beta_{3,2}I_{qnt_vl3}$

qnt_cases : numeric values (1/2/3) corresponding to the categories (Low/Med/High) for the *case* dataset

I_{qnt_vl2} : indicator representing whether *qnt_vl* equals 2.

Coefficient estimates:

qnt cases	Intercept β_0	qnt_vl2 β_1	qnt_vl3 β_2
2	-0.859	1.239	2.042
3	-1.838	1.969	3.605

Exp(Coefficients):

qnt cases	Intercept e^{β_0}	qnt_vl2 e^{β_1}	qnt_vl3 e^{β_2}
2	0.424	3.454	7.704
3	0.159	7.165	36.767

Multinomial logistic regression model

$$\eta(qnt_{cases}) = \beta_0 + \beta_1 qnt_{vl}$$

actual_categories	predicted_categories			Total
	1	2	3	
1	446 63.2 %	192 27.2 %	68 9.6 %	706 100 %
2	189 27.3 %	281 40.6 %	222 32.1 %	692 100 %
3	71 10.3 %	219 31.8 %	398 57.8 %	688 100 %
Total	706 33.8 %	692 33.2 %	688 33 %	2086 100 %

$$\eta(qnt_{cases}) = \beta_0 + \beta_1 qnt_{vl} + \beta_2 qnt_{hosp} + \beta_3 qnt_{cli}$$

actual_categories	predicted_categories			Total
	1	2	3	
1	531 75.2 %	148 21 %	27 3.8 %	706 100 %
2	156 22.5 %	335 48.4 %	201 29 %	692 100 %
3	25 3.6 %	173 25.1 %	490 71.2 %	688 100 %
Total	712 34.1 %	656 31.4 %	718 34.4 %	2086 100 %

Average precision = 53.93%, BIC = 4035.245

Average precision = 65%, BIC = 1657.771

- 1 = Low, 2 = Med, 3 = High
- Including all signals increases precision in **high category** by ~ 13.5%

Variable selection: are all variables significant in the model?

$$\eta(qnt_{cases}) = \beta_0 + \beta_1 qnt_{vl} + \beta_2 qnt_{hosp} + \beta_3 qnt_{cli}$$

- ANalysis Of VAriance (ANOVA): assesses variations in dependent variable distribution across multiple independent variables.
 - By comparing the log-likelihood of the full model with that of a reduced model
- $H_0: \beta_1 = \beta_2 = \beta_3 = 0$
- A small p-value indicates improved model fit.

ANOVA test result: all three signals Viral load, CLI, Hosp are significant in the model

Research Findings

- The availability of supplementary datasets enhances the effectiveness of modeling.
- District-level analysis enables statistical testing to be conducted effectively.

Future Directions

- Retrospective analysis for building forecasting models.
- Clustering algorithms like hierarchical clustering based on categorical indicators.
- Continue exploring other categorical indicators such as phase-based categories.

Key Takeaways

Projecting future cases precisely is impossible and unnecessary.

Even without perfect projections, we can confidently draw conclusions:

- Case rates have rebounded slightly higher after prolonged decline and plateau period
- Hospitalization rates remain in slow decline
- Most indicators still point to continued plateaus
- Long term projections that assume a seasonal trend in the winter show impact of vaccine coverage and slow vs. fast evolution of immune escape
 - Broad annual vaccination campaign reduces hospitalizations by 27% over 2 years

Model Updates

- Projected Trajectories from previous rounds remain on target, no new projections made this round

Questions?

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